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TOXIC EPIDERMAL NECROLYSIS

A REPORT OF FOUR CASES

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In February 1956 we published a report of our first case of epidermolysis resembling scalding in an African male.[1] In November 1956 Lyell[2] described 4 British cases of the same type and suggested the name 'toxic epidermal necrolysis'.

It would seem that toxic epidermal necrolysis should be classified as a variant of erythema multiforme in which the epidermis is the target for the toxaemic onslaught. It can hardly be in doubt that toxins are the etiological basis for this disease. The striking difference between toxic epidermal necrolysis and all the other forms of erythema multiforme, including the Stevens-Johnson[3] syndrome, is the remarkable, sudden, painful epidermo-dermal cleavage which results in secondary formation of 'bullae' due to collection of fluid between the epidermis and dermis, followed by rapid peeling of most of the skin, exposing tender, raw, pink, oozing surfaces.

We now report 4 more cases of this condition—3 in African men and 1 in a Cape Coloured woman:

CASE 1

E.F., an African male convict aged 20 years, was admitted in a semi-stuporous state to the Dermatology ward of the Groote Schuur Hospital on 1 July 1954. He was unable to tell us his story, but his warder informed us that he was serving an outdoor hard-labour sentence and had been perfectly well until 29 June, when he complained of pain in his eyes, a sore throat and a rash. There was no history of his having taken any drugs.

On admission, the temperature was 105°F, pulse rate 100 per minute and respirations 25 per minute. There was a generalized haemorrhagic eruption consisting of purple macules 5-10 mm. in diameter. The epidermis around the neck was lying loosely over the dermis and fluid had collected between the two layers giving, at first sight, an impression of bullous formation. The epidermis had peeled off the cheeks, anterior chest wall and scrotum. Muco-pus was pouring from the eyes, but there was no actual bullous involvement of the conjunctivae nor was there photophobia. A haemorrhagic ulcerative stomatitis was found. There was a balanitis with a purulent sub-preputial discharge but no urethritis or retention of urine, the urinary output remaining normal throughout his stay in hospital.

His general condition was that of a man in the terminal stages of a fulminating disease, with hyperpyrexia, tachycardia and rapid noisy respirations. He could only just be roused out of his stupor and was unintelligible in his responses to questioning.

Next day (2 July), he became comatose, still retaining the swallowing reflex, however. The respiratory rate increased. The epidermis was easily peeled in sheets from the underlying dermis of the face, neck and trunk and could be removed with slight pressure from any part of his body except the scalp and pubis, leaving raw, red, slightly oozing surfaces.

Special Investigations

Wassermann reaction positive. Blood pressure 110/60 mm. Hg.

Blood: Haemoglobin 6·0g.%. Smear normocytic, hypochromic. Leucocytes 12,000 per c.mm., (polymorphs 19%, monocytes 39%, lymphocytes 42%). Platelets present.

1 *July:* Blood urea 140 mg.%. Serum sodium 132 mEq., potassium 3·5 mEq., chloride 92 mEq., CO_2 51·5 vols.%.

2 *July:* Blood urea 55 mg.%. Serum sodium 130 mEq., potassium 4·2 mEq., chloride 92·5 mEq., CO_2 56 vols.%.

3 *July:* Blood urea 60 mg.%. Serum sodium 131 mEq., potassium 4·7 mEq., chloride 88·5 mEq., albumin 4·6g.%; globulin 2·4 g.%.

Urine: No porphyrins. Specific gravity 1,024. Albumin +.

Progress and Treatment

Immediately after the patient's admission to the ward an intravenous drip was set up, at first containing potassium chloride, ACTH, Terramycin, Plebex and Redoxon in dextrose-saline. Later he was given intravenous serum and Amigen. In spite of the anti-shock measures, the blood pressure fell during the last 12 hours of his life and he developed jerky movements of the right arm which were attributed to cerebral irritation. He died on 4 July 1954.

Summary of Post-mortem Findings

Apart from the striking loss of epidermis from most of the body and of mucous membrane from the tongue and buccal surfaces, the purulent conjunctivitis, the balanitis, and a commencing bilateral basal bronchopneumonia, no macroscopic or microscopic abnormalities were found in any other organs. Sections of the cerebral cortex, midbrain, cervical cord, meninges, kidneys, myocardium, pancreas, liver and adrenals showed no

histological changes; and cultures of the liver, spleen and subepidermal fluid failed to demonstrate the presence of bacterial or viral infection. Sections of skin from the chest showed complete dermo-epidermal cleavage at the junction of the epidermis with the dermis which was characterized by a notable absence of cell infiltration in the papillae, though there was a moderate degree of round-cell infiltration about the appendages. Changes in the epidermis consisted of separation of the cells in the stratum corneum together with a diffuse disruption of prickle cells and their intercellular bridges in the stratum malpighii, leading to varying degrees of cyst formation, the vesicles appearing to have erupted downwards towards the basal layers of the epidermis. The dermo-epidermal cleavage was limited to the junction zone and did not extend downwards along the necks of the pilo-sebaceous tracts.

CASE 2

H.M., an African male carpenter aged 48 years, was admitted to the Dermatology ward of the Groote Schuur Hospital on 28 July 1954. His doctor gave the information that he had had an attack of erythema multiforme in 1947, after taking a proprietary aperient containing phenolphthalein. Four days before his admission in July 1954 he had again taken some laxative pills which, the manufacturers informed us, contained phenolphthalein and aloin. That night he was unable to sleep because of shivering attacks and a generalized painful sensation in the skin. Next morning he noticed dusky red patches scattered over the body and several large 'blisters' containing clear fluid. His only other complaint was dysuria, though there was no urethritis nor was there retention of urine.

On admission, the temperature, pulse and respiration rates were normal and the patient was not acutely ill nor was he shocked; he was, however, in very great pain, which he said was localized in his skin and which made him very reluctant to move about in bed. Skin lesions involving the enitre body, apart from the scalp, consisted of flat, well-defined, dusky purple areas, 5-10 mm.

Fig. 1. Case 2. Showing the loose flaccid collections of fluid on the arm.

in diameter. In the axillae and groins and over the anterior aspects of the trunk and thighs, the epidermis was unattached to the dermis and in some areas flaccid bullae had formed; slight pressure on these caused the fluid to raise further peripheral epidermis (Figs. 1 and 2). Large areas were completely denuded, revealing

Fig. 2. Case 2. Showing the loosened wrinkled epidermis.

pink surfaces equisitely tender to the touch and exuding profuse amounts of serum sufficient to keep the bed sheets wet. The conjunctivae and buccal mucosa were not involved. There was a small area of ulceration on the scrotum and the glans penis was acutely inflamed.

Special Investigations

Wassermann reaction negative, B.P. 160/110.

Blood: Hb. 15 g.%. Smear normocytic, normochromic. Leucocytes 8,400 per c.mm. (polymorphs 67%, lymphocytes 20%, eosinophils 12%, monocytes 1%). Platelets seen. Total serum proteins 6 g%, chlorides 101 mEq., CO_2 58·5 vols.%.

Urine: No porphyrins. No abnormal constituents.

Unfortunately consent for a skin biopsy was not obtained.

Progress and Treatment

Immediately after the patient's admission oral therapy was instituted, consisting of cortisone, 75 mg. 6-hourly; potassium chloride; Terramycin, 500 mg. 6-hourly; and a high-protein diet. In addition he was given 7 pints of Dextran intravenously in the first 36 hours. After 2 days on this regime the epithelial denudation had extended and he was still losing copious amounts of serum from the raw areas. On the advice of a surgical colleague accustomed to dealing with extensive burns and scalds, thick, firm bandages were applied in the hope of checking the outpouring of serum. An ointment consisting of Terramycin and balsam of Peru in sterile vaseline was spread on butter muslin, gently laid on the denuded parts and firmly bound thereto with layers of cotton wool and gauze bandages; this was left *in situ* for 5 days, only the outer coverings being changed when they became sodden. By the 5th day in the ward (2 July) the patient was very much better; his pain had disappeared and no more serum was oozing through the bandages. The dose of cortisone was decreased at the rate of 25-50 mg. a day and on 9 July he was

discharged; the whole skin surface was then intact, the extensive raw areas having covered themselves with healthy though depigmented epithelium.

CASE 3

D.N., an African male aged 45 years, employed as a packer at the docks, was admitted to the Dermatology ward of the Groote Schuur Hospital on 4 March 1956. He had been admitted once before in June 1955, with a diagnosis of Stevens-Johnson syndrome following the ingestion of a proprietary aperient containing phenolphthalein. The present attack was, however, far more severe and differed from the first typical Stevens-Johnson episode in several ways. Three days before the second admission he had taken some 'blood purifying' pills and that same night had developed a generalized eruption which was at first associated with itching but not with pain. The eyes and mouth became sore. There was no urethral discharge, dysuria or retention of urine.

On admission, the temperature was 100°F, pulse rate 88 per minute. There was a purulent conjunctivitis, though no conjunctival bullae were seen, and the patient was not photophobic. The lips and buccal mucosa showed a haemorrhagic, ulcerative stomatitis. The entire surface of the body apart from the scalp was covered with large, flaccid sacs of clear fluid which hung in big bags from the under surfaces of the arms and thighs and which extended easily, on the slightest pressure, along the lines of cleavage. The only other abnormal findings were a collapsing pulse and auscultatory signs of mitral stenosis and aortic incompetence; he was not in congestive cardiac failure, nor was there any evidence of subacute bacterial endocarditis.

Special Investigations

Wassermann reaction negative. B.P. 130/75.

Fig. 3. Case 3. Note the close resemblance to severe scalding.

Fig. 4. Case 4. The buttocks bear the main brunt of epidermolysis. A large haemorrhagic area may be seen on the left side of the chest.

Fig. 5. Case 4. 12 Days after admission. The necrotic epidermis has all been shed. Healthy unscarred epidermis now covers all the hitherto denuded areas.

Blood: Hb 13 g.%. PCV 45%. Leucocytes 8,000 per c.mm. ESR 20 mm. per hour (Westergren).

Urine: No abnormal constituents.

Permission for skin biopsy was not obtained.

Progress and Treatment

Oral therapy with cortisone, 75 mg. 6-hourly, potassium chloride, Aureomycin and a high-protein diet was instituted forthwith. The sacs of fluid were ruptured and the resultant raw areas (Fig. 3) were firmly bandaged as in case 2. On 6 March progress had not been as good as had been expected, and so the cortisone was replaced by oral hydrocortisone, 100 mg. 6-hourly. The dose was gradually reduced during the ensuing few days and by 12 March there was a vast improvement, which continued until 21 March, when the patient was discharged cured.

CASE 4

E.M., a Coloured housewife aged 64 years, was admitted to the Dermatology ward of the Groote Schuur Hospital on 26 April 1957. She had had an ulcer on her left ankle for 7 years. In January 1957 her doctor had given her penicillin ointment, which she had used on the ulcer for 3 months in spite of its having caused a severe dermatitis of the surrounding skin. She was given one intramuscular injection of penicillin in January and on the following day she developed 'blisters' over the whole body and these persisted for some time. On 22 April another practitioner gave her an injection of penicillin and within a few hours the whole body became purple and began to itch; the skin came away in large sheets. At this stage the pruritus was replaced by severe pain.

On admission, the temperature was normal, pulse rate 80 per minute, respirations 25 per minute. The patient was too ill and in too much pain to be thoroughly examined; the skin was completely detached from the lower back, buttocks, flexor surfaces of the thighs and legs, axillae, arms and forearms (Fig. 4). The epidermis on the dorsum of the hands and feet was intact, but was unattached to the underlying dermis and there was an accumulation of pink haemorrhagic fluid between the two layers, looking

as though the patient was wearing rubber gloves containing liquid. The palms and soles were unaffected.

There was a haemorrhagic, crusted blepharitis though no conjunctivitis or photophobia was present; the eyelids presented a purple, ecchymotic appearance. The lips were covered with haemorrhagic crusts but there was no involvement of the buccal mucosa.

The patient had complained of dysuria for some months; this, however, had not been aggravated by her present illness and her urinary output remained good throughout her stay in hospital.

Special Investigations

Wasserman reaction negative. B.P. 170/100.

Blood: Hb 14 g.%. PCV 44%. Leucocytes 20,000 per c.mm. (polymorphs 80%, lymphocytes 19%, monocytes 1%). ESR 16 mm. per hour (Westergren). Blood urea 37 mg.%. Serum albumin 4·1g.%. Globulin 2·3 g.%. Thymol turbidity 1. Zinc turbidity 9.

Urine: No porphyrins. No abnormal constituents.

Skin biopsy from axilla: Included in the specimen are representative portions of epidermis and corium. The basal cells of the epidermis show some hydropic degeneration and there is also some hyperkeratosis with increased numbers of effete melanin-containing cells lying in the keratin. The most striking changes are observed in the corium: these consist of pronounced sub-epidermal oedema and a moderate perivascular and peri-adnexal infiltrate of eosinophils, lymphocytes, and histiocytes. In addition, the upper corium contains large numbers of melanophores.

Culture of organisms from the skin: M. pyogenes aureus sensitive to Novobiocin, less so to Chloromycetin.

Progress and Treatment

Oral therapy was immediately instituted and consisted of prednisone, 15. mg. 6-hourly, Achromycin, a high-protein diet, and pethidine for the severe pain. A powder containing chloramphenicol was dusted onto the extensive raw areas, followed by tulle gras, cotton wool and firm bandaging, all left *in situ* for 3 days. On 29 April there was still considerable seepage of pink, haemorrhagic serum through the dressings, which were then removed, revealing the raw areas, which had not extended and which looked considerably healthier, though showing no signs of epithelization as yet. The patient was free from pain and could slowly turn herself in bed.

On 1 May the temperature rose to 101°. As there were no signs of pulmonary or urinary infection, this pyrexia was attributed to toxic absorption from the still fairly extensive denudation, though no sepsis was evident and the buttocks were by this time completely covered with thin, pink epithelium. The oral antibiotic was changed from Achromycin to Novobiocin and the dose of prednisone was reduced to 12½ mg. 6-hourly.

On 4 May removal of the bandages revealed complete re-epithelization of all the affected parts, with no scarring. The temperature was normal and from then on the progress of recovery was uninterrupted. The doses of prednisone and of Novobiocin were daily decreased so that, by 13 May, the patient was perfectly well and fit to be discharged (Fig. 5).

COMMENT

It might be argued that all our cases should have been diagnosed as the Stevens-Johnson syndrome and, indeed, they resembled that disease more than any other but for the sudden painful dermo-epidermal cleavage resulting in secondary 'bullous' formation which has not been seen in our many cases of Stevens-Johnson syndrome.

From our studies the histological picture of toxic epidermal necrolysis is not typical of erythema multiforme or of Stevens-Johnson disease, in which the major changes start in the dermis. In our cases the necrotic lytic process occurred in the epidermis, the dermis showing only varying degrees of oedema.

In all our patients except the stuporous convict there was a definite history of the administration of drugs known to be toxic to certain individuals. In the case we reported in 1955[1] the patient had taken oil of chenopodium; phenolphthalein had been taken by case 2 and presumably by case 3 shortly before the onset of the illness; and case 4 had been using penicillin topically for months and had received an intramuscular injection of penicillin a few hours before her illness started. It is possible that she exemplified a sort of Sanarelli-Schwartzmann phenomenon, months of cutaneous sensitization to penicillin leading to an explosive necrotic reaction when the same substance was given parenterally.

Pemphigus is easily distinguished from toxic epidermal necrolysis by the sudden fulminating appearance of large areas of epidermolysis in the latter after a brief prodromal period suggestive of acute toxaemia. The necrolysis occurs at the dermo-epidermal junction and not superficially in the stratum malpighii, where the bullae of pemphigus arise. The rapid, uninterrupted and permanent healing that takes place in epidermal necrolysis, when it is heroically treated, is quite unlike the story of pemphigus.

In pellagra, bullous and raw areas resembling scalds are sometimes seen, but are found in conjunction with other evidence of chronic malnutrition—pigmentation, follicular keratosis, glossitis, diarrhoea and liver dysfunction.[4] No hepatic changes were found in our two cases on whom autopsies were done.[1]

Dr. J. S. Harington,[5] of the Department of Insecticidal Biochemistry of the Council for Scientific and Industrial Research, drew our attention to the work of Clare[6] and Louw[7, 8, 9] on a hepatotoxic disease in sheep following the ingestion of a plant, the active principle of which causes acute photosensitization and icterus, with sloughing of the skin.

SUMMARY

An acute toxic syndrome of sudden dermo-epidermal cleavage resembling scalding is described, with reports of 4 illustrative cases. In the authors' view this syndrome should be broadly classified as a variant of erythema multiforme, though the points of differentiation set it apart from the well-known forms of this group of diseases.

We wish to express our thanks and appreciation to Dr. R. Schapera and to Dr. J. C. Uys for their valuable contributions in the histological studies in these cases, and to Mr. B. Todt for the photographs.

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EDITORIAL

COPING WITH INFLUENZA

Since the pandemics of 1890 and 1918, still in living memory, the threat of influenza pestilence has been constantly before mankind. Now that an influenza pandemic has become an actuality, and its spread throughout most of the world probable, it comes to assuage the apprehensions of epidemiologists rather than to exacerbate them; for while there can be no certainty that the prevailing mild strain of infection will not become graver by mutation, hopes may reasonably be entertained that this disaster will not occur. At any rate, the plans which our health authorities must make should be based on the more optimistic apprehension of a mild epidemic of influenza.

Should the infection reach South Africa the emergency that might arise would probably consist of a widespread outbreak of a catarrhal fever demanding confinement to bed and simple medical treatment. Amongst the patients with milder attacks severer cases would occur, relatively small in proportion but possibly large in actual numbers. The severe cases would demand closer medical and nursing attention and a proportion would urgently need admission to hospital, some by reason of severity alone and others because of lack of reasonable accommodation at home. Especially amongst non-Europeans there is a large population whose home conditions are totally unsuitable in the event of illness. The outbreak might be expected to last for a few weeks, and apart from the medical, nursing and pharmaceutical professions the brunt of the emergency would be borne by the local health, hospital and relief authorities assisted by voluntary agencies such as Red Cross, St. John's, Noodhulpliga, Salvation Army, etc. In urban areas the necessary organization can best be left to the municipal authorities who, however, will need all the support that can be given by other official and voluntary bodies.

In former pandemics a varying degree of disorganization of services took place. In some households so many members fell ill that none were left to maintain essential household services and to care for the sick. To cope with this situation, home-visiting services and local depots and feeding centres were needed. In urban areas these should be under municipal coordination, and motor transport should be provided.

If a hospital emergency arose the first step would be to

VAN DIE REDAKSIE

OM GRIEP DIE HOOF TE BIED

Sedert die pandemies van 1890 en 1918, nog binne menseheugenis, was die mensdom gedurig bewus van die bedreiging van griepepidemies. Noudat 'n grieppandemie 'n werklikheid geword het en die verspreiding daarvan oor die grootste gedeelte van die wêreld waarskynlik is, kom dit om die vrees van epidemioloë te verlig eerder as om dit te vererger; want, alhoewel daar geen sekerheid is dat die heersende ligte graad van infeksie nie ernstiger sal word deur mutasie nie, kan die verwagting redelikerwys gekoester word dat hierdie siekte nie sal voorkom nie. In elk geval, die voorsorgsmaatreëls wat ons gesondheidsbeamptes moet tref, behoort op die meer optimistiese begrip van 'n ligte epidemie van griep gebaseer te word.

Indien die infeksie na Suid-Afrika versprei, sal die noodtoestand wat mag ontstaan, waarskynlik in die vorm van 'n wydverspreide uitbreking van 'n kataragtige koors wees, wat vereis dat die pasiënt in die bed moet bly en eenvoudige geneeskundige behandeling ontvang. Onder die pasiënte wat die siekte in 'n ligte graad sal kry, sal ernstiger gevalle voorkom, betreklik klein in verhouding maar waarskynlik groot in werklike getalle. Die ernstige gevalle sal noukeuriger geneeskundige aandag en verpleging verg en vir 'n gedeelte van hulle sal toelating tot 'n hospitaal dringend noodsaaklik wees, sommige net as gevolg van die hewigheid van die siekte en andere weens gebrek aan behoorlike huisvesting. Veral onder die nie-blankes is daar 'n groot aantal wie se huislike toestande geheel en al ongeskik is in geval van siekte. Dit kan verwag word dat die uitbreking 'n paar weke sal duur en afgesien van die geneeskundige, verplegings- en farmaseutiese beroepe, sal die plaaslike gesondheids-, hospitaal-, en onderstandsbeamptes, bygestaan deur vrywillige organisasies, soos byvoorbeeld die Rooi Kruis, St. Johns, die Noodhulpliga, die Heilsleër, ens., die spits moet afbyt gedurende die noodtoestand. In stedelike gebiede kan die nodige organisasie met gerustheid in die hande van die munisipale beamptes gelaat word, maar hulle sal egter al die bystand wat ander offisiële en vrywillige organisasies kan verleen, nodig hê.

In vorige pandemies het daar heelwat wanorde van dienste geheers. By sommige huisgesinne het so baie gesinslede siek geword, dat niemand oorgebly het om die nodige huiswerk te verrig en om die siekes te versorg nie. Om hierdie toestand die hoof te bied, was dit nodig om huisbesoekdienste, plaaslike depots en voedingsentrums in die lewe te roep. In stedelike gebiede behoort hierdie dienste met die samewerking van die munisipaliteite te geskied en motorvervoer behoort verskaf te word.

Indien 'n hospitaalnoodtoestand ontstaan, sal die eerste voorsorgsmaatreël wees om die beste gebruik te maak van die bestaande hospitale deur sover nodig en moontlik

make the best use of existing hospitals by restricting ordinary admission to emergency cases, so far as necessary and possible, thus providing hospital accommodation for those influenza patients for whom it might be essential. Normally cases of infectious disease are not admitted to the Provincial hospitals, but in the face of an influenza emergency this restriction should be waived. To make advance provision for temporary hospitals, should existing hospitals prove insufficient, is a formidable task which may be regarded as more than is called for by the apparent threat. During the last war the civilian defence authorities in certain towns made provision for emergency hospitals, and in considering their plans for an influenza epidemic it would be well for the municipal authorities to look into the preparations that were made 15 years ago. Much more is needed to convert a building to a hospital than bedsteads and bedding.

Should the anticipated epidemic be of such magnitude as to require special organization on the part of private medical practitioners and nurses, the organization can well be left to Branches and Divisions of the Medical Association and to the Nursing Association, in cooperation with the municipalities and other organizations concerned. Detailed plans in this respect can only be made when the needs of the situation become apparent.

An influenza epidemic would involve heavy demands on stocks of medicines, such as aspirin and cough remedies and, for pneumonic complications, sulphonamides and antibiotics. The necessary action to ensure that sufficient stocks would be avilable in the country could only be taken effectively by the Union Government or the Provincial Administrations.

Preventive action against the spread of influenza has not hitherto proved effective. Nothing short of the total interruption of human social intercourse could succeed in this. With regard to the use of the vaccine prepared from the specific strain of virus, it is generally recognized that vaccination of the whole community is inpracticable. All schemes for coping with an influenza epidemic are dependent on the necessary personnel—medical, nursing and other—and if the vaccine is available it should be used for the protection of such essential personnel.

gewone toelatings slegs tot noodgevalle te beperk, sodat hospitaalhuisvesting op hierdie wyse aan die pasiënte met griep, vir wie dit noodsaaklik mag wees, verskaf kan word. Gewoonlik word gevalle met aansteeklike siektes nie tot Provinsiale hospitale toegelaat nie, maar met die oog op 'n griepnoodtoestand behoort daar van hierdie beperking afgesien te word. Om vooruit voorsiening te maak vir tydelike hospitale, indien dit blyk dat bestaande hospitale ontoereikend is, is 'n reusetaak wat beskou kan word as meer as wat die waarskynlike bedreiging sal vereis. Gedurende die afgelope oorlog het die burgerlike verdedigingsmag in sekere stede voorsiening gemaak vir noodhospitale, en volgens maatreëls wat destyds vir 'n griepepidemie getref is, sal dit die munisipale beamptes baat om in te gaan op die voorbereidings wat 15 jaar gelede getref is. Wanneer 'n gebou in 'n hospitaal omskep word, is daar heelwat meer as net beddens en beddegoed nodig.

Indien die verwagte epidemie so ernstig is dat dit spesiale organisasie aan die kant van private geneeshere en verpleegsters verg, kan dit met gerustheid aan die Takke en Afdelings van die Mediese Verenigings en die Verplegingsvereniging, in samewerking met die munisipaliteite en ander betrokke organisasies, oorgelaat word. Die nodige planne in hierdie verband kan slegs getref word wanneer dit duidelik word wat die toestand vereis.

'n Griepepidemie sal 'n groot aanvraag na voorrade van geneesmiddels, soos byvoorbeeld aspirien en hoesmiddels, en vir longkomplikasies, sulfonamiede en antibiotika, meebring. Die nodige reëlings om te verseker dat voldoende voorrade in die land beskikbaar sal wees, kan slegs op doeltreffende wyse deur die Unie-Regering of die Provinsiale Administrasies getref word.

Dit het geblyk dat voorsorgsmaatreëls om die verspreiding te verhoed, tot nog toe nie doeltreffend was nie. Slegs algehele onderbreking van sosiale menslike omgang kan hierin slaag. Sover dit die gebruik van die entstof, wat van die spesifieke soort virus voorberei word, aanbetref, word dit algemeen besef dat inenting van die hele gemeenskap onpraktïes is. Alle maatreëls wat getref word om 'n griepepidemie die hoof te bied, is afhanklik van die nodige personeel—geneeskundige, verplegings-, en andere—en indien entstof beskikbaar is, behoort dit vir die beskerming van sodanige noodsaaklike personeel gebruik te word.

TASTE, APPETITE, AND THE SELECTION OF FOOD

A symposium devoted to a discussion of taste, appetite and the selection of food was held in the latter part of last year at the Sheffield meeting of the British Association for the Advancement of Science.[1]

In his paper Professor Zotterman, of Stockholm, pointed out that recent advances in electrophysiological technique had revealed many interesting features about the basic problems of taste by direct studies of activity in the taste nerve fibres. Thus advances have been made beyond the older ideas of 4 classes of taste, namely sweet, sour, bitter and salt. Fibres have been demonstrated that respond to acid, and others that respond to salt and acid. It is also believed that mammals, including man, can detect water with their taste buds; warm-blooded animals have specific taste organs or receptors for water. From studies on single-fibre preparations the author and his co-workers have found that even so-called primary taste sensations are composed as a pattern of several types of taste fibre. With electrophysiological methods American workers have demonstrated great species differences in the response of the taste fibres of the chorda tympani. In man direct proof of water fibres is still lacking, and it remains to be demonstrated whether his discrimination between water and weak salt solutions is due to highly sensitive salt receptors alone or to a dual system of salt and water fibres. Studies such as these will give more information on the pattern of the afferent impulses concerned in taste; and, further, by using micro-electrodes to record the activity of single nerve cells in the cortex, information is being gained about the cerebral gustatory mechanism.

J. G. Gordon, of the Rowett Research Institute, discussed

palatability in relation to physiological needs. He indicated that 'palatability' is not to be confused with the palate or with the sense of taste, and that it depends on a number of factors, including touch, smell, taste and vision, these again varying according to the type of animal, activity of senses, hunger, appetite, and psychic factors. The author has studied some of these problems in sheep, cattle, and rats, and concludes that palatibility *per se* is not altogether to be relied on as a reflection of bodily needs. His answer to the saying 'A little of what you fancy does you good' is that it may do you good because you fancy it, but it is doubtful whether you fancy it because it does you good.

In another paper R. Harper considered the psychological aspects of food acceptance, which are many and varied. He showed the difference in approach between the physiologist and the psychologist. The physiologist's approach is exemplified by the electrophysiological investigation of the sense of taste (see above). The psychologist takes everyday experience and behaviour as his starting-point. Harper gave illustrations of certain contemporary psychological approaches to the many problems of food acceptance, and indicated that in the present state of our knowledge many facts of food acceptance cannot be fitted into a physiological framework.

H. N. Munro considered whether we derive greater benefit from a diet if certain nutrients are consumed together rather than at separate meals. He gave a few examples of time factors which influence protein utilization. Thus all the amino acids needed for tissue protein formation must arrive at the tissues simultaneously. Again it has been demonstrated that the presence of carbohydrate with protein in the same meal has a beneficial action on the utilization of the protein, and suggestions have been put forward to explain this effect. Little, however, is known about the interrelation between foodstuffs and further study is needed on the basis of specially designed experiments.

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GENERAL PRACTICE SERIES

DIABETES MELLITUS

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1. *Varieties of Diabetic*

Diabetics vary in type:

1. The commonest are those patients whose diabetes starts in adult life, who are often obese, who do not go into ketosis or coma (but see paragraph 4 of section 15—*Intercurrent Illness*), and who are often relatively resistant to insulin. From the point of view of the metabolic disturbance the diabetes is 'mild'. These patients may be symptom-free or present with the vascular 'complications' of diabetes.

2. Diabetes starting in young people is metabolically more severe. The patient tends to go into ketosis, for the prevention of which insulin is needed and is often life-saving. Such patients are usually insulin-sensitive. This 'young' type of diabetes may sometimes affect older people.

The family history is frequently positive in both varieties (1 and 2).

3. Less commonly the diabetes may be 'secondary' to a variety of rarer conditions. These include chronic pancreatitis, Cushing's syndrome, treatment with cortisone, acromegaly.

We shall refer to these types of diabetes below.

2. *Diagnosis*

1. A patient should not be considered diabetic solely on the grounds of glycosuria.

2. A single trustworthy blood-sugar reading of over 150 mg. per 100 ml. while fasting, or over 200 mg. on venous blood at any time, is diagnostic of diabetes, and a glucose tolerance test is then quite unnecessary.

3. Occasionally during an acute staphylococcal infection, in the course of a meningo-cerebral illness, in acute pancreatitis, during treatment with cortisone, after a severe accident, and in severe thyrotoxicosis, one may find 'temporary diabetes'. Apart from such incidents, once a diabetic, always a diabetic. Occasionally a clinical remission may occur in an established diabetic, but the underlying abnormal state is still present.

4. The glucose tolerance test is of major value in the recognition of the mild diabetic (glycosuria with a single blood-sugar reading not diagnostically raised) and the 'prediabetic'.

3. *Diabetes in Pregnancy*

Diabetes is no bar to pregnancy unless (1) previous pregnancies were complicated by severe eclampsia, or (2) advancing retinopathy with deterioration of vision is present.

Today there is no increased risk to the mother, but there is still great danger to the foetus. The diabetic mother's baby is typically overlarge, fat, oedematous, rubicund and weak, respires with difficulty, is slow to suck, is often born dead or dies within the first 3 days. To help obtain a live child:

1. The mother's diabetes should be well controlled with

* The following articles in the General Practice series, by the same authors, will appear in coming issues of the *Journal:* 'The Thyroid Gland', 'The Pituitary Gland', 'The Adrenal Glands' and 'Diseases of the Gonad'.

diet, together with insulin (or one of the new oral hypoglycaemic agents) if required.

2. The mother should be admitted to a maternity hospital for confinement.

3. Surgical induction of labour or Caesarean section should be performed at the 36-37th week, unless the foetus appears to be of small size.

4. The newborn child should be managed as though it were a weak premature infant.

During pregnancy most type-2 diabetics require more insulin for their control, though this is not invariable. The dosage may need to be altered frequently. Immediately after parturition there is a steep lowering of insulin requirement for a day or two, at which time hypoglycaemia is easily produced. During this period insulin should be given only if it is obviously needed.

The mainstay of treatment of the type-1 diabetic during pregnancy is still dietary, and it is doubly important in diabetics that the weight gain during pregnancy should be closely controlled (a gain of 20 lb in the whole period for a patient of normal frame; preferably no gain at all in the obese person).

Diabetes itself is no bar to lactation. Naturally if the mother is ill with, say, renal disease, then the question is judged on that basis.

4. *Pre-diabetes*

This term is given to the state preceding the development of obvious glycosuria and diabetic symptoms, during which a woman may nevertheless show evidence of impending diabetes. She is liable to the same complications of pregnancy, with a high rate of foetal and post-natal loss, and the same fat, over-sized babies.

Pre-diabetes is no longer purely a matter of theoretical interest, but has practical implications for the practitioner:

1. It should be suspected as the cause of any unexplained stillbirth, especially of repeated stillbirths, and especially if the foetuses are large (e.g. over 10 lb in weight). Glycosuria during pregnancy should also be suspect, and not merely passed off as caused by a lowered renal threshold, without investigation.

2. Pre-diabetes can often be diagnosed with certainty by means of specially designed glucose tolerance tests, or from the pancreas of the stillborn if it is available for pathological study.

3. To prevent further foetal loss any future pregnancy should be treated as if the mother were an established diabetic.

5. *Diet*

There are 2 main objects of dietary regimes:

1. To reduce the weight of the obese 'mild' diabetic. Here the obesity is the primary disorder, and the diabetes can usually be left to look after itself. In fact it is questionable whether insulin should be used in this type of diabetic, except in occasional emergencies, until the obesity has been corrected.

2. In the insulin-requiring diabetic, to render the control of the diabetic state easier and more accurate, to help prevent both ketosis and hypoglycaemic attacks.

One hopes incidentally that the better control afforded by diet will also lessen the incidence or severity of later vascular complications. The general principles of the diet are:

1. To reduce the carbohydrate intake to between 100 and 200 g. per day (depending upon total allowed calories). This is done largely by completely omitting most foodstuffs containing concentrated carbohydrate, such as sugar, jam, honey, cake, pastry, dumplings, sweets and chocolates, by restricting the staple dietary items such as bread, potatoes, rice and mealies and by allowing unlimited cabbage, cauliflower, squash, pumpkin, marrow, lettuce and tomatoes.

2. To allow a total calorie intake that will maintain weight at 5-10% below the mean standard for the patient's age.

3. To make up the remainder of the diet with fat and protein.

4. To eat regular meals at frequent intervals. If insulin is being taken, meals must never be missed.

5. To adjust calorie intake at specific meals to the insulin dosage and to physical exertion (this may require specialist advice in difficult cases).

6. *Insulin*

Unless absolutely impossible, the 'severe' insulin-requiring diabetic should be controlled in hospital. The 'lente' (zinc suspension) insulins are now adequate for the control of almost all diabetics. The practitioner need only be acquainted with the use of 'lente' itself, while realizing that 'ultralente' and the old 'zinc protamine' have a very prolonged action up to 36 or 48 hours. The majority of diabetics can be well controlled on lente insulin only, in moderate single daily doses, and if such control is not obtained then a diabetic expert's advice is recommended.

The only other insulin the practitioner needs to use is ordinary soluble insulin. This, and this insulin only, should be used in patients who are in ketosis or impending diabetic coma.

An important practical point for the patient is that the site of insulin injection must be changed daily. All areas of the body which have a fair amount of subcutaneous tissue are suitable, and the same site should not be used more than once a year. Further, the injection should not be too superficial.

7. *Oral Hypoglycaemic Agents* (*D 860, Tolbutamide*)

Active oral antidiabetic substances are now available, are safe, and are suitable for use in the *'mild', older, type-1 diabetic only*. Even then obesity must be remembered to be the primary enemy, when present. There is no reason why D 860 ('Rastinon', 'Orinase', 'Artosin') should not be used by the practitioner in the mild case in place of insulin, but on no account should a severe diabetic of the young type be allowed to attempt such replacement. The results of long-term therapy with these agents are not yet known.

8. *Meaning of 'Control' in Diabetes*

Ideal control means no glycosuria and a blood sugar within normal limits at all times. This is usually impossible to attain, because of the danger of hypoglycaemic reactions if aglycosuria is insisted upon. In the 'severe' case, tests of urine sugar should be made at different times of day, and provided these are nearly all green or blue (Benedict), with only an occasional yellow, one is usually satisfied. Blood-sugar estimations should be occasionally performed as an additional check, particularly since some patients may show no glycosuria and yet have high blood sugars, while others

pass sugar and yet have normal blood levels. Such alterations of renal threshold need specialist investigations.

9. *Coma*

If the practitioner is certain that his patient is in diabetic coma or near-coma he should (1) give 100 units of soluble insulin immediately, and (2) arrange urgent admission to the hospital with the best possible facilities.

If it is impossible to admit the patient to hospital, the practitioner must look elsewhere for advice, since it would take too much space here. (On request, we will gladly send any practitioner a copy of the scheme for treatment used at the Groote Schuur Hospital.)

If the patient is a known diabetic, taking insulin, the practitioner must be quite certain that the coma is not hypoglycaemic, since more insulin in such a state may be fatal. In the differentiation of the two comas, it may be stressed that the onset of hypoglycaemia is rapid, and may be sudden, whereas the ketotic coma is a gradual affair, usually a matter of slow worsening over days—certainly hours. If doubt still exists, application of the biochemical tests referred to in paragraph 16 should settle matters. It is possible for a patient in hypoglycaemic coma to have glucose in his bladder, this having been excreted from the kidneys at an earlier period. Finally, if there is still uncertainty between hypoglycaemia and ketotic coma, intravenous glucose may be given. Here it must be remembered that coma from long-acting insulin may be resistant to glucose, and sometimes large amounts (even up to 1,000 g. or more) are necessary. After a patient has recovered from hypoglycaemic coma he should take some carbohydrate at least every 2 hours for 24 hours, as the long-acting preparations may still have a hypoglycaemic effect. For a few days after a hypoglycaemic attack insulin requirements may fluctuate. Finally one must attempt to ascertain the cause of the coma, e.g. too much insulin, undue exertion or the missing of a meal, as some adjustment in insulin dosage may be necessary.

The effect of *exercise* in helping to use up more sugar than usual and so tending to produce hypoglycaemia is important for the insulin-requiring diabetic to remember. Befo undertaking any unwonted exertion, he should eat an extra snack, which should contain some protein or fat in addition to carbohydrate (e.g. a meat sandwich).

10. *Neuropathy*

1. The symptoms of diabetic 'neuritis' are rarely felt in the arms—pain in shoulders and arms is usually due to some other condition.

2. The diabetic should never be vitamin-deficient, and no vitamin is of the slightest value in the treatment of diabetic neuropathy.

3. The only treatment is better control of the diabetes.

11. *Eyes of the Diabetic*

There are many serious ophthalmic complications of diabetes. A few points of practical importance may be made:

1. *Refractive changes* (presumably due to osmotic changes in the media) occur at the onset of diabetes and at the beginning of treatment. It follows therefore that new spectacles should not be prescribed until the diabetes is stabilized.

2. An attempt at really exact control should be made if *retinal disease* is advancing. There is no other hope.

3. *Glaucoma* is a frequent and serious complication. It is easily overlooked by any but the ophthalmologist. Any ocular complaint in a diabetic must therefore be taken seriously, and usually demands expert advice.

12. *Kidneys of the Diabetic*

Diabetics, even when well treated, are prone to urinary-tract infection, which leads to chronic pyelonephritis.

Symptoms may be very slight; hence:

1. Catheterization should be avoided; if essential, really effective asepsis must be maintained.

2. Treatment of pyelitis should be vigorous, and controlled by bacteriological diagnosis and microscopic evidence of cure. Renal infection is of far more practical importance to the practitioner than the specific diabetic kidney (Kimmelstiel-Wilson lesion).

13. *Feet of the Diabetic*

All diabetics should be warned never to cut their own corns or calluses or perform any other 'surgical' exercise on their feet. Shoes must not be tight. Feet must be kept clean and free from fungus infections. A trained chiropodist should perform necessary pedicure (any diabetic clinic worthy of the name has a chiropodist in attendance). These points are important and may prevent gangrene and save a leg or even a life.

14. *Operations in Diabetics*

Diabetes is no bar to anaesthesia or operation if otherwise indicated. Certainly if ketosis is present, this should be dealt with first, by vigorous fluid and insulin therapy. In the 'mild' diabetic, not taking insulin, nothing whatever need be done. In the 'severe' young type of insulin-requiring diabetic the easiest plan is probably to stop the patient's regular insulin the day before the operation and replace with soluble insulin as necessary. The urine should *not* be kept sugar free, since the only real bugbear to the anaesthetist is hypoglycaemia. In emergencies, intravenous glucose drip can always be used to counteract any circulating insulin.

15. *Intercurrent Illness*

This is a matter of great practical importance to the practitioner, in the case of the 'severe' diabetic.

1. In no circumstances should insulin be stopped; often it will have to be increased, and extra soluble insulin added.

2. If possible, the patient's calorie intake should be maintained near to the normal level. A fluid diet can be based on the following:

Milk	130 calories in 7 oz.
Sugar	112 calories in 1 oz.
Benger's, Ovaltine, Horlick's etc.	about 44 calories in ½ oz.

3. If the patient really refuses all food or if it is contra-indicated for medical reasons, it is quite a good plan to give him a half of his normal insulin dosage and add soluble insulin later if the urine indicates that it is necessary.

4. Occasionally the 'mild' diabetic goes into ketosis and even coma in the presence of an acute infection. Insulin will be required if the urine shows +++ sugar *and* ketones.

16. *Simple Biochemical Tests*

It is well known that Benedict's test on urine is non-specific, and may give a positive result with lactose, fructose and other reducing substances, while a very annoying doubtful positive often occurs if urates are present in any quantity. The new

paper tests (e.g. Testape) are quite specific and indicate glucose only. Because of this they should be most useful for the practitioner, although from a semi-quantitative point of view they are less reliable than Benedict's test (as in a known diabetic). Tablet tests (e.g. 'Clinitest') will remain useful when boiling is difficult, and are to be interpreted in the same way as the Benedict (or Fehling) reaction.

It must be remembered that Rothera's (nitroprusside) test is a very sensitive one for urine ketones, and easily becomes positive with acute infections, vomiting or mild starvation in diabetics or non-diabetics. A positive Gerhardt (ferric chloride) test calls for action, but neither test has any diabetic significance unless the urine sugar is also 3+ positive. A positive Gerhardt with less sugar than this may result from salicylate administration, when the reaction will remain after boiling the urine with a drop of nitric acid (whereas with ketones, the test becomes negative); with salicylates Rothera's test is negative.

In emergency when diabetic coma is suspected, a Rothera test may be done on the blood-serum or plasma, just as it is done on urine. If the coma is diabetic the test will be strongly positive.

VAGINAL SMEARS IN A CASE OF OVARIAN AGENESIS (GONADAL DYSGENESIS)

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n reports on cases of ovarian agenesis there are records of he vaginal smears[1-4] but no detailed descriptions are given. De Allende[5a] describes the atrophic smears and their response to therapy in 2 cases of primary amenorrhoea with retarded secondary sexual development, and also in bilateral oophorectomy.

When Miss F.F. was diagnosed as ovarian agenesis it was found (on rectal examination) that she had an infantile vagina and uterus. It was therefore decided:

1. To make daily serial vaginal smears for examination in order to establish variations in the cell counts.
2. To treat her with hormones and assess the effect on the vaginal cytology.
3. To determine the genetic sex from both the exfoliated vaginal cells and a biopsy of the vaginal epithelium.

Unfortunately, owing to her early demise, the second intention could not be carried into effect.

CLINICAL HISTORY

The patient was 20 years 11 months when she was admitted to hospital in November 1956, primarily for investigation of her cardiac condition. When she was 11 years old she suffered an attack of rheumatic fever which resulted in aortic stenosis. This accounted for all her symptoms.

At the age of 12 her mother noticed that her growth was retarded and that there were no signs of development of secondary sex characteristics. When she was 15 years old she had a menstrual period for 1 day, followed a few months later by a second period of the same duration. On both occasions the blood loss was scanty. There are recorded cases of ovarian agenesis with irregular bleeding.[3, 6,7]

In April 1954 F.F. was diagnosed as a case of panhypopituitarism. She was given injections over a period of 8 months. Initially she had 4 intramuscular injections (1 a week) of oesterogens. This was then followed by weekly injections of chorionic gonadotrophins. The injections were stopped and, soon after, she had a slight blood loss for 1½ days, a period of amenorrhoea (duration unknown), and then a second scanty bleeding. There was no change in her external appearance. She had not undergone any further treatment before admission to hospital on 8 November 1956.

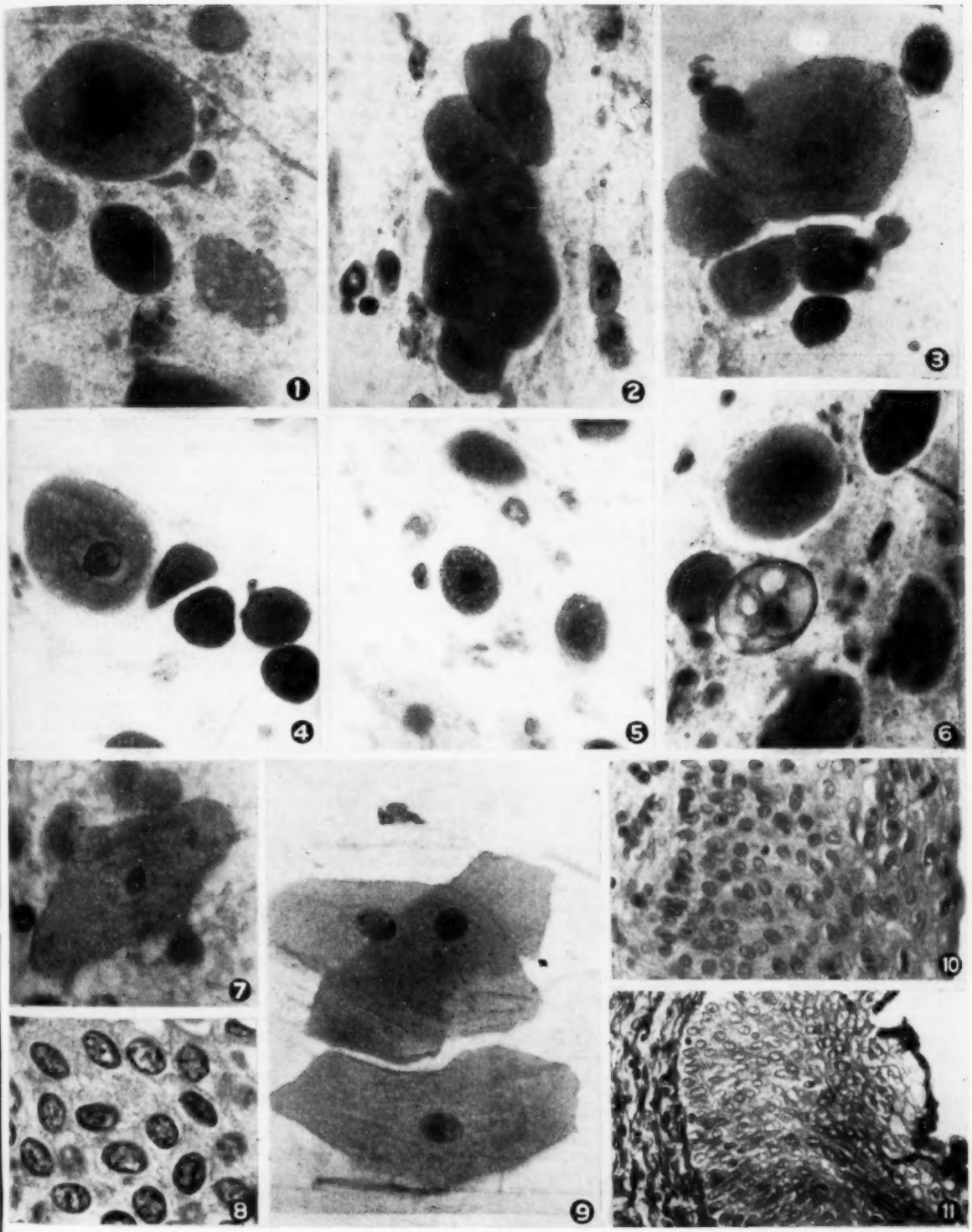
On examination she presented the following features: Short stature 56¼ inches (142·6 cm.), weight 73¾ lb. (33·5 kg.), marked cubitus valgus, absence of breast development, no axillary hair, scanty pubic hair, and infantile external genitalia. The clinical diagnosis was therefore ovarian agenesis with superimposed rheumatic aortic stenosis.

Unfortunately the patient's condition deteriorated and she developed congestive cardiac failure. She died of acute cardiac failure suddenly on 18 January 1957.

Hormonal Assays. Four specimens of urine were sent at different times for Follicle Stimulating Hormone assays. The first specimen was reported as less than 6 mouse units, the second and third were both more than 48 mouse units and the last specimen was less than 6 mouse units. This last assay was performed on a specimen voided 3 days before death when the patient was in congestive cardiac failure. Unfortunately only one set of oestrogen estimations was done, the volume of urine being 420 c.c. The result was as follows: oestriol 1·0 microgram (normal 10 micrograms), oestrone 0·8 microgram (normal 5-6 micrograms), oestradiol 0·0 microgram (normal 1-2 micrograms).

The *genetic sex* was diagnosed as male from studies on the epidermis.

Fig. 1. Large outer basal cell and small inner basal cell. Oil.
Fig. 2. Cluster of inner basal cells at bottom, and middle basal cells at top. Oil.
Fig. 3. Binucleate outer basal cell. Oil.
Fig. 4. Vacuoles in cytoplasm of middle basal cell, perinuclear vacuole and vacuole in nucleus. Oil.
Fig. 5. Inner basal cell with small vacuoles in cytoplasm. Nucleus shrunken and pyknotic. Oil.
Fig. 6. Large vacuoles in middle basal cell. Oil.
Fig. 7. Large cornified cell with pyknotic nucleus, perinuclear halo and cytoplasmic granules. Oil.
Fig. 8. Vaginal epithelium nuclei of cells from transitional zone showing the absence of 'sex' chromatin. Oil.
Fig. 9. Precornified cells, 2 with vesicular nuclei, 1 with pyknotic nucleus. In the two vesicular nuclei there is no 'sex' chromatin. Oil.
Fig. 10. Vaginal epithelium showing, from right to left: narrow superficial zone, wide transitional zone, germinal layer. × 430 Haematoxylin and Eosin.
Fig. 11. Vaginal epithelium showing distinct basement membrane and lamina propria. × 344 Shorr stain.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Post mortem examination showed the ovaries to be rudimentary cords, and the histological features were similar to those described by other workers.[2,4,8] No definite follicles were found in either ovary. There was a dense connective-tissue stroma, and large nests of hilar cells. The diagnosis was thus confirmed.

CYTOLOGY

Material and Technique

Vaginal smears had been made daily from 15 November to 13 December, excluding 3 days on which the patient was subjected to various other examinations. The smears were prepared by the usual method, fixed in equal parts of 95% alcohol and ether, stained with Harris haematoxylin followed by Shorr stain in separate solutions.[5b] Fields from all parts of each smear were studied, and a minimum of 400 cells per smear was counted.

Post mortem: the vagina was fixed in Bouin's solution, dehydrated and embedded in paraffin wax. Sections were cut at a thickness of 6 microns. Some sections were stained with haematoxylin and eosin in order to study the morphology of the epithelium (Fig. 9), and also for the purpose of diagnosing the genetic sex (Fig. 11). Other preparations were stained with Shorr's stain by the same technique as that used for the vaginal smears (Fig. 10). For further studies on the nuclei sections stained with Heidenhein's iron haematoxylin were used.

Macroscopic Appearance

The vaginal secretion was scanty, cream coloured, markedly mucoid and fairly viscous. Although it adhered to the sides of the pipette, once expelled it spread easily. Because the mucus was so tenacious some slides were uneven in thickness, the central portions being very dense. There was no obvious macroscopic variation over the 28-day period.

Microscopic Appearance

The general impression was that it was a 'dirty' smear.[5c] The majority of the cells were enmeshed in the viscid mucus. On the periphery of the smears and in some fields they were evenly distributed and discrete. Owing to disintegration there was abundant cellular debris, consisting of nuclear and cytoplasmic remnants; free nuclei also were scattered in the mucus. Numerous leucocytes were present in all the smears. The vaginal cells appeared degenerate and 'woolly' both cell and nuclear outlines being poorly defined. The nuclear detail in many cells could not be seen because the nuclei exhibited such intense basophilia. Cell counts were performed but the percentages of the different cell types present showed little variation.

Cell Structure

In this description Graham's terminology is used with modifications.[8]

Basal (deep) cells predominated (Figs. 1 and 2) accounting for approximately 90% of the total cell count; the range was between 85 and 94%. The presence of basal cells has been noted by other observers.[1-4] Three sizes were distinguished. The small inner basal cells measured 14 × 13 microns in diameter, the cytoplasmic rim being equal to one-half or less of the nuclear diameter. The diameters of the medium-sized basal cells were 24 × 23 microns, the cytoplasmic rim being at least equal to the nuclear diameter. The large outer basal cells had diameters of 35 × 28 microns, the cytoplasmic rim being equal to at least 1½ times the nuclear diameter. The cells were usually round, although the larger ones showed a tendency to be oval. The cytoplasm was basophilic and opaque, being less opaque in the larger cells.

The nuclei were large, central and generally basophilic, many displaying an intense basophilia. Where the chromatin network could be distinguished it was fine and delicate. There was much variation in nuclear appearance, some nuclei being pyknotic and shrunken, others fragmented and scattered in the cytoplasm as coarse irregular granules. A third variety was the smooth swollen nucleus in which the chromatin appeared woolly. The nuclei in these cells were greatly enlarged and occupied almost the whole cell, being surrounded by only a narrow rim of cytoplasm. Occasionally binucleate cells were seen, with delicate vesicular nuclei (Fig. 3).

A notable feature was the marked vacuolation of both cytoplasm and nuclei (Figs. 4-6). The vacuoles varied in size and number. In some cells the entire nucleus was replaced by a single large vacuole surrounded by the dark basophilic nuclear rim. In others numerous small vacuoles were clustered in the cell cytoplasm.

Scattered in the smears was an occasional intensely eosinophilic cell, also from the deeper layers of the vaginal epithelium. It was small in size and oval or round. The eosinophilic nucleus stained intensely and the cytoplasm was coarse and granular. These cells did not contain vacuoles.

The basal cells occurred singly or adhered in clusters on the periphery of the smears. The following were their average proportionate numbers in the total deep-cell count: middle basal 49%, inner basal 43%, outer basal 7%.

The superficial cells consisted of cornified and pre-cornified cells, and accounted for 10-15% of the total cell count.

The cornified cells (Fig. 7) were large, eosinophilic, polygonal cells with thin cytoplasm. Their borders were either smooth and regular or wrinkled and folded. They presented 3 varieties of nucleus. Some cells had pyknotic shrunken nuclei with or without a perinuclear halo. Others had much larger vesicular nuclei with a fine chromatin network; in these the cytoplasm displayed a paler eosinophilia. In the third variety no nucleus was evident and the cytoplasm contained scattered coarse irregular nuclear fragments, or there was a ghost nucleus. The cornified cells occurred singly or in clumps and varied from 2 to 10% of the total cell count. In a few smears they accounted for less than 2%.

There were clusters of orange-red cells without nuclei and also fragments of cornified cells. These had probably come from the lower third of the vagina and were not included in the count.

The pre-cornified cells (Fig. 9) were large, squarish or polygonal, with delicate transparent pale basophilic cytoplasm. They were frequently wrinkled and folded (Fig. 9). The majority had large vesicular nuclei with a delicate chromatin network. These cells were commonly arranged in sheets of 4-6 or more and were often distorted. The remaining pre-cornified cells had either smaller pyknotic structureless nuclei or, as was evident in a few cells, nuclear fragments scattered in the cytoplasm.

In the total cell count the pre-cornified cells averaged 8%, with variations from 3 to 10%; of these 0·5 to 2% had pyknotic nuclei.

Table I shows the percentage occurrence of each cell type in the smears.

Genetic Sex

The exfoliated vaginal cells with vesicular nuclei were found to be chromatin negative (Fig. 9). Carpentier *et al.*[10] quoted 7 cases, '4 listed as ovarian agenesis, whose vaginal smears revealed the genetic sex as male'. Post-mortem sections of the vagina confirmed these findings in both the epithelial (Fig. 8) and muscle cells. Sohval *et al.*[11] state that 'the female nuclear morphology can be revealed in the vaginal epithelium as readily as in the epidermis'.

Section of the Vaginal Epithelium

In the vagina (Figs. 10 and 11) the transitional zone formed two-thirds of the whole epithelium. The number of cell layers varied from 6 in the thinnest portions to 25 in the deep epithelial papillae. The greater part of this zone was occupied by layers of large round to columnar cells with vesicular nuclei. These cells corresponded in appearance with those found in the inner and middle basal cells of the smear. In the few superficial layers of this zone the cells were lying parallel to the basement membrane. Their nuclei were large, vesicular and oval. These cells corresponded in type with the outer basal cells of the smear. A notable feature was the folding of the nuclei in many cells in this zone. The superficial zone consisted of 4-5 rows of flattened cells with smaller irregular, more densely staining, flatter nuclei. These layers accounted for the pre-cornified and cornified cells. These histological appearances were similar to those found in sections of atrophic vaginal epithelium taken from girls of 3½ and 5 years.[12] Wilkins and Fleishman[4] describe the vaginal mucosa from a vaginal biopsy in one of their cases as 'prepubertal'.

DISCUSSION

The most significant finding was the presence of cornified cells in all the vaginal smears. They varied in frequency from 2 to 10%. The fact that the patient had had hormonal therapy can be discounted, as the injections were discontinued 23 months previously. Therefore it appears that oestrogens were not entirely absent but were being secreted in minimal quantities, sufficient to cause cornification of a small number of the superficial vaginal cells. No definite follicles could be found in either of the two gonads. The assumption follows that the oestrogens which were being secreted were produced elsewhere.

Basal cells are rarely seen in normal smears during the reproductive period but they were the predominant cell type in all these smears (90%). This indicated a markedly atrophic state of the vaginal epithelium. The sudden steep drop in the number of outer basal cells (Table I) showed that maturation of cells had been grossly impeded subsequent to the middle basal-cell stage.

TABLE I

Cell Type	*% of Total Cell Count*
Superficial cells	
Cornified cells	2 - 10%
Precornified cells	3 - 10%
Basal cells	84 - 95%

Basal-cell Type	*% of Total Basal Cell Count*
Outer basal cells	7% average
Middle basal cells	49% average
Inner basal cells	43% average

On histological section the vaginal epithelium resembled that which is seen in children before the onset of the menarche. This confirmed the findings in the smears.

The exfoliated cells were in a degenerate state, as evidenced by the abnormal nuclei and marked cytoplasmic vacuolation. This is probably due to oestrogen deficiency, for similar cytological appearances are found in other conditions characterized by low oestrogen levels.

There were 3 varieties of cornified cells. It appeared as though the pre-cornified cell with a vesicular nucleus might pursue any one of the following paths:

precornified cell with vesicular nucleus	→ precornified cell with pyknotic nucleus	→ precornified cell with nuclear fragments
↓	↓	↓
cornified cell with vesicular nucleus	→ cornified cell with pyknotic nucleus	→ cornified cell with nuclear fragments

Finally there was no evidence of cyclical activity over the 28-day period, but minor fluctuations did occur in the cell counts.

SUMMARY

1. Cell counts on vaginal smears from a patient with ovarian agenesis were performed over a period of 28 days.

2. Minor fluctuations occurred in the percentages of the cell types. Basal cells averaged 90%. Superficial cells averaged 10%, of which 5% became cornified. These data indicated a slight degree of oestrogenic activity.

3. The smear was of the atrophic degenerate type.

4. The genetic sex was male.

It is hoped to give a full clinical report with post-mortem findings in a later publication.

My thanks are due to Dr. Roy Morris for kindly allowing me to investigate his patient. I am also grateful to Prof. R. A. Dart, in whose department this work was performed, to Mr. Dry for his assistance and photography, and to Dr. D. Bronks for her advice and criticism.

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HAEMORRHAGIC INFARCTION OF THE OVARY IN EARLY PREGNANCY

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Ovarian infarction occurring in early pregnancy, unassociated with pelvic infection or other obvious local causes, has to the knowledge of the authors not been reported in the literature. The following detailed report of such a case is therefore submitted.

CASE REPORT

Present Illness

C.S., a Coloured female aged 40 years was admitted to Groote Schuur Hospital, Cape Town, for the first time on 21 June 1956, with the provisional diagnosis of ectopic pregnancy. She stated that she was 3 months pregnant, her last menstrual period having occurred on 20 May 1956. She was quite well until 14 days before admission, when she experienced a sudden severe hypogastric pain which caused her to faint. The pain radiated to the upper abdomen and lasted for one day, after which it gradually subsided. She did not vomit, nor did she experience any bowel or urinary disturbance or notice any vaginal bleeding. She felt very weak and remained in bed for one week. Six days before admission she vomited on one occasion, and 3 days later she again experienced a sudden severe pain in the right iliac fossa, but did not faint. The pain gradually spread over the hypogastrium and remained localized to this region up to the time of her admission to hospital. Following the onset of the pain she vomited persistently but again did not experience vaginal bleeding, bowel or urinary disturbances. The practitioner who was consulted the day after the onset of the second episode of pain diagnosed pyelitis, and treated her with an alkaline mixture and sulphonamide tablets, also administering morphine and pethidine.

Previous History

She was a gravida11, having between 1942 and 1953 had 8 normal full-term deliveries, 1 premature delivery and 2 miscarriages. At the age of 24 she underwent an appendicectomy, and in 1950 a right-sided mastoidectomy was performed for acute mastoiditis. Cortical-vein thrombosis, which followed 3 weeks after the operation, resulted in a transient right hemiparesis; from this she had fully recovered during the past 2 years.

Physical Findings

On admission she was in obvious pain and looked pale. Her temperature was 100°F, blood pressure 110/60 mm. Hg. and pulse rate 96 per minute. The feet and ankles showed pitting oedema. No abnormalities were detected in the respiratory and cardiovascular systems. Abdominal palpation revealed great tenderness and guarding in the hypogastrium, especially in the right iliac fossa; there was a suspicion of a vague mass rising out of the pelvis on the right side.

On vaginal examination, the cervix was soft and normally situated and there was marked tenderness in all the fornices, particularly the right adnexal region; again a vague mass in the right adnexal region was palpated. The uterus was enlarged to the size of an 8 weeks gestation. There was no bleeding from the cervix, nor was there any abnormal discharge.

Special Investigations. Haemoglobin 8·5 g.%; leucocyte count 8,400 per c.mm.; blood group A, Resus negative. Urinalysis, no abnormal constituents.

Operation

In view of the acute abdominal emergency presented by the patient, the differential diagnosis of ectopic pregnancy, or alternatively of torsion of a right-sided ovarian cyst associated with intra-uterine pregnancy, was made, and it was decided to examine the patient under an anaesthetic as a preliminary to possible operation. One pint of blood was administered before operation. Under anaesthesia the uterus was found to be anteverted, soft, and enlarged to the size of an 8 weeks gestation. The left adnexa were normal. In the right adnexal region, antero-lateral to the uterus, was an elongated firm mass approximately 3½ by 1½ inches in size. The mass, which was mobile and palpable independent of the uterus, was thought to be ovarian in origin. As these findings supported the diagnosis of a twisted ovarian cyst associated with pregnancy, the abdomen was opened by the median subumbilical route. A normal pregnant uterus and normal left adnexa were revealed. The left ovary did not contain the corpus luteum of pregnancy. In the right adnexal region, the tumour felt vaginally was found to be a considerably enlarged ovary antero-lateral to the uterus. It was mobile and had a bluish-black appearance. There was no evidence of torsion. The ovarian ligament, the tube and the infundibulo-pelvic ligament on that side were normal. The hilum and the meso-ovarium contained dilated and thrombosed veins. The infundibulo-pelvic and broad

Fig. 1. The external and sectioned surfaces of the ovary are demonstrated. The haemorrhagic ovarian substance and the large corpus luteum of pregnancy can be seen on the cut surface. Scale in inches.

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ligaments were then palpated to determine whether the thrombosis had extended to these veins. However, they were normal. A right oöphorectomy was performed.

Pathological Findings

Macroscopically, the ovary presented as a flattened ovoid mass of tissue (Fig. 1). The external surface was deeply haemorrhagic and wrinkled. Except for groups of thrombosed vessels that could be recognized towards the hilum, as well as a cystic structure which measured 1·9 cm. in diameter and resembled corpus luteum, the gross detail of the cut surface was largely obliterated by extensive haemorrhage. Histologically (Fig. 2), the large veins were much more prominent than usual, being distended by red coagulation thrombus. The walls of many were intact and in most the only abnormality was a perivascular infiltrate of polymorphonuclear leucocytes. In others the cellular outlines were smudged and blurred due to fibrinoid necrosis, and scattered masses of chromatin were all that remained of the cells. The perivascular exudate of polymorphonuclear leucocytes was more intense around the more severely affected vessels, and in some these extended into the necrotic wall and into the thrombus.

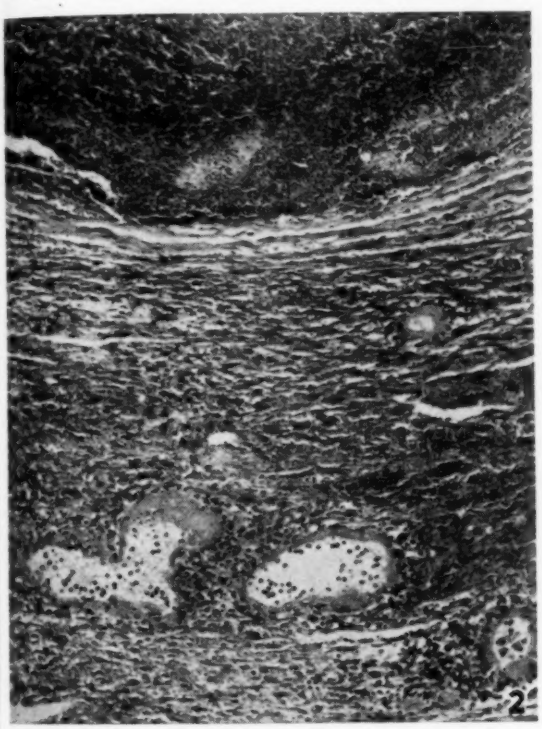

Fig. 2. A large ovarian vein filled with coagulation thrombus is present as well as several necrotic venules free of thrombus. The stroma is necrotic, shows evidence of recent haemorrhage and contains a perivascular infiltrate of acute inflammatory cells. Haemotoxylin and eosin × 60.

The small veins and venules showed striking necrotizing and inflammatory changes, but as these were confined to the areas of ovary showing evidence of infarction, they had presumably shared in this process.

Only occasional arteries in the areas of infarction were involved but the majority were intact and showed neither inflammation, necrosis nor haemorrhage.

The haemorrhage did not involve the ovarian stroma uniformly. There were foci where it was quite massive and the stromal cells were separated by sheets of red cells; in other areas the cells were separated mostly by oedema fluid containing scanty red cells. The perivascular exudate occurred in the surrounding stroma to a lesser degree, and in only one or two areas did it exist without being related to damaged adjacent vessels. In the areas of maximal stromal haemorrhage many stromal cells had shrunken pyknotic nuclei indicating that they too had undergone necrosis. This became less apparent towards the tunica albuginea, where many of the cells appeared viable. The serosal lining cells of the ovary had been activated and appeared cuboidal or columnar.

In addition, a large corpus luteum of pregnancy and several corpora albicantia were present. The haemorrhage also extended into the theca interna of the corpus luteum, and in one small focus the cells had undergone necrosis.

Post-operative Course

Progesterone was administered by 30 mg. daily injections. The post-operative course in hospital was uneventful and on the 10th post-operative day the patient was discharged with instructions to take 40 mg. daily by mouth. However, she discontinued taking the tablets and 8 days after her discharge from hospital she aborted. She was re-admitted and the abortion completed by curettage.

DISCUSSION

The gross and microscopic appearances of the ovary are those of incomplete haemorrhagic infarction with hilar-vein thrombosis, the most striking changes being severe congestion and widespread interstitial haemorrhage with necrosis. These findings indicate that the infarction is largely due to venous rather than to arterial occlusion. The tendency would be to associate the venous thrombosis with the infarction, but there are other factors which suggest that both the infarction of the ovary and the venous thrombosis may have been secondary to sudden and prolonged venous obstruction.

As the venous thrombosis constitutes a presenting feature, the elucidation of its pathogenesis and of its relation to the infarction is of primary importance.

In the ovary, as elsewhere, the factors which predispose to thrombosis may conveniently be considered under three headings constituting the so-called 'Virchow's Triad'; these are (*a*) provocative lesions of the vascular intima, (*b*) changes in the velocity and character of the local blood stream, and (*c*) changes in the constituents of the blood. As a predisposing cause the last-named—changes in the constituents of the blood—may be dismissed without further consideration. The blood count and the absence of clinical findings related to blood diseases, immediately rule out such blood dyscrasias as polycythaemia vera, leukaemia or thrombotic purpura—conditions which are known to be associated with visceral thrombosis. Neither do provocative intimal lesions that may predispose to thrombosis exist in the form of primary vascular disease. Although many vessels show necrosis it is clear that the lesion forms part of the infarction noted in the ovary and thus was not primary in nature. The inflammatory exudate noted in the region of the vessels is in response to the thrombosis and tissue necrosis.

The last factor which may be operative in intravascular thrombosis is concerned with changes in the velocity and character of the local blood stream. The stasis produced by partial or complete occlusion due to torsion of the ovarian pedicle will adequately fulfil these conditions. At operation, however, there was *no* evidence of torsion. Even so, the relatively long history, extending over a period of 14 days, and the episodic nature of the pain, might both be accounted for by intermittent torsion. In fact the history is in keeping with possibly three episodes of torsion, one of which may have been followed by thrombosis of the ovarian vein.

Further evidence in support of torsion as a cause of venous occlusion rather than primary thrombosis is the fibrinoid necrosis of the smaller vessels which are free of thrombus, the infarction and the extensive haemorrhage. Neither of these can be adequately accounted for by incomplete thrombosis alone.

It seems thus reasonable to infer from the available evidence that initally torsion produced obstruction of the ovarian venous return, which resulted in partial haemorrhagic infarction of the ovary and thrombosis of some of the vessels; and that at the time of operation the torsion had been rectified but the thrombosis naturally persisted. The only significant fact against this theory is the apparent absence of the usual lesions in the ovary which might favour torsion. No ovarian mass or cyst was present, and the ovarian ligament and infundibulo-pelvic ligament appeared normal and not unduly lengthened. It is doubtful if the corpus luteum of pregnancy was of sufficient size to produce conditions favouring torsion. But to reject the hypothesis of torsion in the absence of a physical cause for it, is to imply that one always finds a cause for torsion or volvulus. That this is not the case is sometimes illustrated by volvulus of the testis and sigmoid colon where no predisposing cause may be demonstrated.

SUMMARY

1. A case of haemorrhagic infarction of the ovary occurring in early pregnancy is described.

2. Although no evidence of torsion was present at operation, the history and the histological appearances of the ovary indicate that intermittent torsion may possibly have been the cause of the incomplete ovarian infarction.

3. To the knowledge of the authors no similar case has been reported in the literature.

We wish to thank Prof. J. T. Louw and Prof. J. G. Thomson for their helpful advice and criticism during the compilation of this paper, Dr. N. Cloete, Superintendent of the Groote Schuur Hospital, for his permission to publish this case, and Mr. B. Todt for the photographs.

BLOOD ALCOHOL CALCULATIONS MADE EASY

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Legislation regarding misconduct due to drunkenness has been in force in the Union for a considerable time, but provision for the taking of blood samples from persons suspected of being under the influence of liquor has only been introduced recently.[1] This provision has brought to the fore the importance of the determination of blood alcohol by chemical analysis. One should however not forget that the blood-alcohol level is a test which does not replace the clinical examination, but which supplements it.

It is comparatively simple for the practitioner, in the quiet of his own rooms, to calculate alcohol absorbed into the body tissues, blood alcohol % and 'tots' taken; but it can become complicated under embarrassing circumstances, e.g. when standing in a witness box. With this in view, it was decided to simplify the calculation so that all figures can be read off instantaneously.

For calculating the total amount of alcohol absorbed into the body tissues at the time of taking the blood sample [2,3] the following formula is used:

$$A = p \times c \times r, \text{ where}$$

A = total weight of alcohol in grams absorbed into the body tissues;
p = weight of subject in kilograms;
c = blood alcohol $\% \times 10$;
r = ratio of concentration of alcohol in the body to that in the whole blood. In man this is considered to be 0·68 or 0·7 and for purposes of calculation this factor has been taken as 0·67.

The above formula can now be converted as follows:

$$A' \text{ c.c.} = \frac{p \text{ (lb.)} \times \text{blood alcohol } \% \times 10 \times 0{\cdot}67}{2{\cdot}204 \times 0{\cdot}8}, \text{ where}$$

A' = total volume of alcohol in cubic centimetres absorbed into the body tissues;
r = 0·67;
2·204 = lb. per kilogram;
0·8 = grams alcohol per cubic centimetre.

Thus

$$A' \text{ c.c.} = \frac{p(\text{lb.}) \times \text{blood alcohol } \% \times 6{\cdot}7}{1{\cdot}7632}$$
$$= p(\text{lb.}) \times \text{blood alcohol } \% \times 3{\cdot}8$$

From this equation it is possible to set out blood alcohol % against body-weight (lb.) in tabular form, with the relevant volumes of alcohol absorbed into the body tissues, as given in Table I.

TABLE I

Blood Alcohol %	*c.c. Alcohol absorbed in the body*										
0·05	27	29	30	32	34	36	38	40	42	44	46
0·06	32	34	36	39	41	43	46	48	50	52	55
0·07	37	40	43	45	48	51	53	56	59	61	64
0·08	43	46	49	52	55	58	61	64	67	70	73
0·09	48	51	55	58	62	65	68	72	75	79	82
0·10	53	57	61	65	68	72	76	80	84	87	91
0·11	59	63	67	71	75	79	84	88	92	96	100
0·12	64	68	73	78	82	87	91	96	100	105	109
0·13	69	74	79	84	89	94	99	104	109	114	119
0·14	75	80	85	91	96	101	106	112	117	122	128
0·15	80	86	91	97	103	108	114	120	125	131	137
0·16	85	91	97	103	109	116	122	128	134	140	146
0·17	90	97	103	110	116	123	129	136	142	149	155
0·18	96	103	109	116	123	130	137	144	151	157	164
0·19	101	108	116	123	130	137	144	152	159	166	173
0·20	106	114	122	129	137	144	152	160	167	175	183
0·21	112	120	128	136	144	152	160	168	176	184	192
0·22	117	125	134	142	151	159	167	176	184	192	201
0·23	122	131	140	149	157	166	175	184	192	201	210
0·24	128	137	146	155	164	173	182	192	201	211	219
0·25	133	143	153	162	171	181	190	200	209	219	228
	140	150	160	170	180	190	200	210	220	230	240
	Body-weight in lb.										

The range of body weights is given from 140 to 240 lb., which should cover the weight of most subjects. The blood-alcohol percentage figures from 0·05 to 0·25 were chosen because the figure for 'under-the-influence-of-liquor-and-unfit-to-drive-a-car' would fall somewhere in between.

According to Mellanby,[1] the average rate of combustion of alcohol in man is 8 g. or 10 c.c. per hour for adults. Thus, by combining Table I with an Alcohol Elimination Graph, which is shown on this page, calculation becomes unnecessary. The 'tot' equivalent, as given in this graph, is calculated as follows:

1 'Tot' = 1·25 fl. oz. = 35·5 c.c. or approximately 35 c.c.
Spirits contains 43% by volume of alcohol. Hence
1 'tot' = 35·5 × 0·43 = 15·25 c.c. alcohol or approximately 15 c.c.
1 pint of beer = 5% alcohol by volume = 29 c.c. alcohol.
1 bottle (24 fl. oz.) of wine = 14% alcohol by volume = 95 c.c. alcohol.

The value of table and graph can best be illustrated by considering a hypothetical case:

Mr. A. is charged by the Crown with driving a car while under the influence of liquor. At 10 p.m. he had left a public bar, which he had entered at 9 p.m. At 11 p.m. he was arrested while driving his car. He admitted to the Police that he had been drinking between 9 p.m. and 10 p.m. and that he had taken 3 'whiskies'.

At 11·30 p.m. he was clinically examined by the District Surgeon, who assessed his weight at 170 lb. and took a blood sample for analysis.

The Government Analyst reported to the Police that Mr. A's blood gave a blood-alcohol figure of 0·16%.

From Table I it is evident that a blood-alcohol percentage of 0·16 at a body-weight of 170 lb. equals 103 c.c. of alcohol absorbed in the body.

Mr. A. was clinically examined 2½ hours after he commenced drinking. By consulting the Alcohol Elimination Graph, one finds that during this period 25 c.c. of alcohol had been eliminated from the body by combustion.

(Draw a line, parallel to the slanting lines on the graph and cutting the horizontal axis at the 2½-hour point. This line will then cut the vertical axis at 25 c.c.)

Mr. A. therefore drank 103 c.c. − 25 c.c. = 128 c.c. of alcohol. According to the figures on the vertical axis of

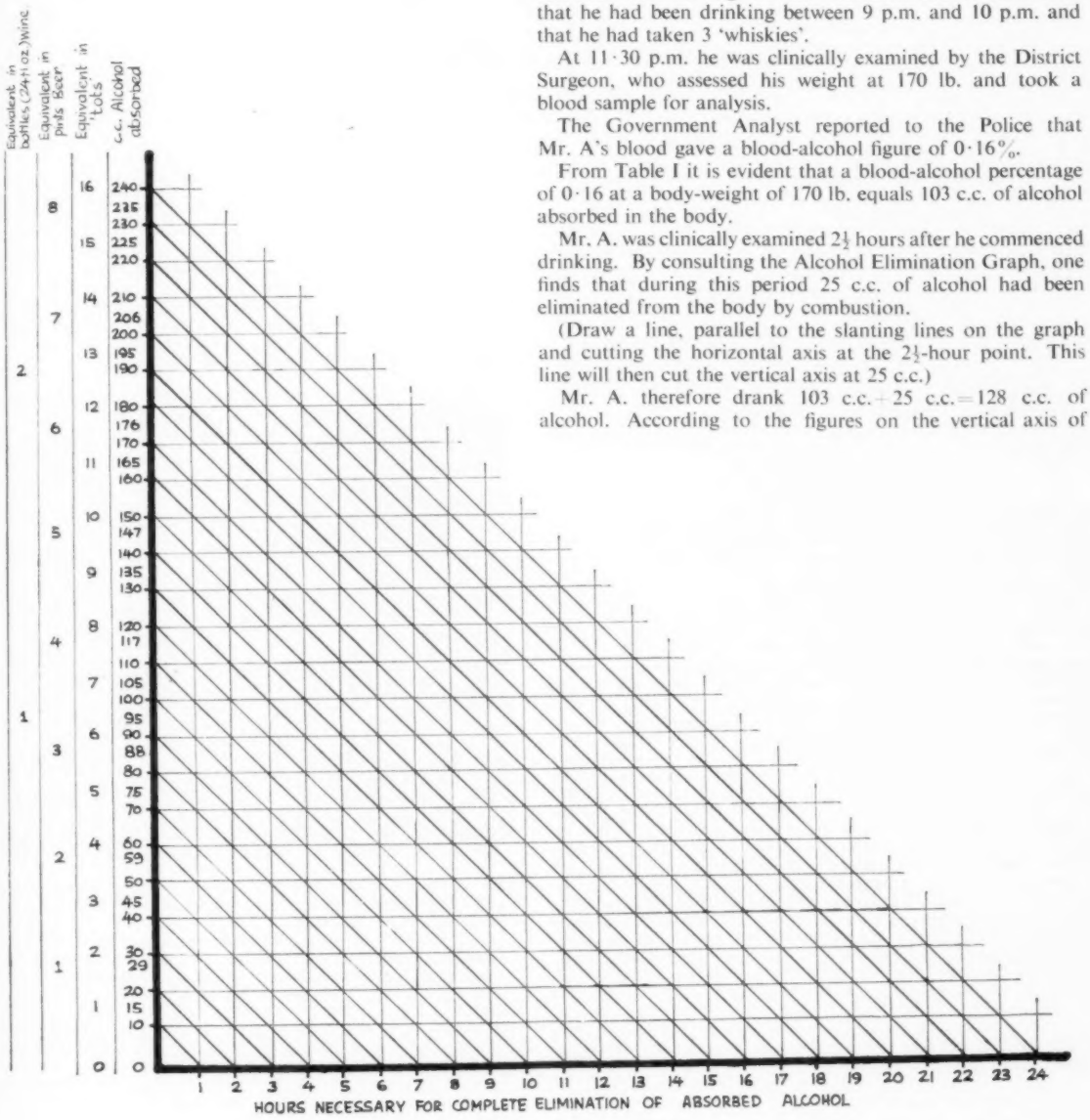
Equivalent in bottles (24 fl. oz.) Wine
Equivalent in pints Beer
Equivalent in 'tots'
c.c. Alcohol absorbed
HOURS NECESSARY FOR COMPLETE ELIMINATION OF ABSORBED ALCOHOL

Fig. 1. Alcohol elimination graph.

this graph, this is slightly more than 8 'tots', which immediately belies Mr. A's statement made to the Police. Furthermore, 12·8 hours would be required to eliminate this alcohol by combustion in man.

At the trial, the District Surgeon was asked by the defence what the blood-alcohol % would have been if Mr. A. had partaken of only 3 'tots' of whisky: 3 'tots' of whisky contain 45 c.c. of alcohol. During the period which elapsed before the taking of the blood sample, 25 c.c. of alcohol was eliminated by combustion. This then leaves 20 c.c. of alcohol. By consulting Table I, one sees that the blood alcohol percentage would thus have been below 0·05 (in this case it is 0·03).

The writer wishes to thank the Chief, Division of Chemical Services, for kind permission to publish this article.

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TUMOURS OF THE MANDIBLE, 1828 AND 1957

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Kimberley

The case of adamantinoma of the mandible, described by Mr. T. Schrire in the *South African Medical Journal* of 18 May 1957, brought back memories of my student days in the University of Edinburgh in 1932. In the Anatomy Museum there was a painting (Fig. 1) of a man with a huge tumour of the jaw—Robert Penman—, a mounted specimen of the tumour, which had been removed by James Syme, the great Edinburgh surgeon, and a photograph of Penman, taken 30 years after the operation. Permission to photograph these items was granted me by Professor Brash, Professor of Anatomy, and Mr. E. R. Jamieson (of 'Wee Jimmie' fame) and two of the photographs, taken in 1932, are produced.

I found that the story of Robert Penman and his tumour and operation had been described by the surgeon (Syme) in the Edinburgh Medical and Surgical Journal in 1828. And here is the case report of what became known as 'The Penman Case' by Mr. J. Syme, as I then copied it out in the Medical Library of Edinburgh University.

THE PENMAN CASE

Though excision of the lower jaw has of late years been frequently performed by various surgeons at home and abroad, I flatter myself that the following case will be read with interest, since the tumour which was the subject of it is, I have reason to believe, the largest that has been removed by this operation.

In the beginning of July I was requested by Dr. Sibbald to examine a tumour which he was anxious to have removed, provided it could be done with safety to the patient. He told me that, while on a professional visit to Coldstream, he had seen the unfortunate person in question, and learned the following particulars of his case.

Between 8 or 9 years ago, Robert Penman, then 16 years old, noticed a hard swelling of the jaw on the outer side of the grinding teeth of the lower jaw. The swelling was not painful, but gradually increased. When it attained the size of an egg, he applied to a surgeon of the neighbourhood who extracted 3 of the adjoining grinders. It then grew more rapidly and having at length become so large as a double fist, induced him to repair to the Royal Infirmary of this city, where it was removed i.e. cut off from the bone. The wound did not heal, and the actual cautery was repeatedly applied in vain to make it do so. After remaining 8 months in the Infirmary, he returned home, but finding the tumour regularly and rapidly increasing, he, 2 years afterwards, came again to Edinburgh, and consulted a distinguished operating surgeon, who declined making any attempt towards his relief. He went home with the fearful prospect of a certain, lingering and painful dissolution, and it was after 3½ years spent in this miserable state, that Dr. Sibbald happened to see him. Though the tumour was then nearly 3 times larger than it was when the patient last quitted Edinburgh, Dr. Sibbald felt persuaded that it was still within the reach of surgery and, therefore, encouraged the young man to come once again to town, which he accordingly did.

Though prepared for something very extraordinary and frightful, I certainly was astonished at first sight of the patient. The representation prefixed to this paper may give some notion of what mere words are altogether inadequate to express.

The mouth was placed diagonally across the face, and had suffered such monstrous contortion as to measure 15 inches in circumference. The throat of the patient was almost obliterated, there being only about 2″ of it above the sternum, so that the cricoid cartilage of the larynx was on a level with that bone. When the tumour was viewed in profile, it extended 8″ from the front of the neck. It completely filled the mouth and occupied all the space below it, from jaw to jaw. The tongue was thrust out of its place, and lay between the teeth and cheek of the right side. The only portion of jaw not implicated in the disease was the right ramus and base of the same side, from the tricuspid teeth backwards. The tumour, where covered by the integuments, was

Fig. 1. Clinical portrait in oils made for Mr. James Syme by an unknown contemporary artist, of the patient Robert Penman before operation.
Fig. 2. Skeleton of portion of mandible removed which contained the tumour. [This appearance is identical with that of a massive adamantinoma, and the subsequent history accords with this diagnosis—*Editor, S. Afr. Med. J.*].

uniformly very firm, and for the most part distinctly osseous. The part which appeared through the mouth was a florid, irregular fungous-looking mass of variable consistence, from which an alarming haemorrhage had occasionally occurred; and for the last 3 or 4 weeks there had been almost a daily discharge of blood to the extent of 1 or 2 ounces. Notwithstanding the great bulk of the tumour, the patient could move his jaw pretty freely in all direc-

tions. With the exception of the disease, now described, Penman enjoyed good health. He was a tall, well made though much emaciated, intelligent young man and possessed an uncommon fortitude.

Having carefully examined the tumour, I undertook to remove it; and this proposal meeting with the approbation of Dr. Abercrombie and Professor Ballingal, was with the assistance of the latter gentleman, carried into execution on the 7th of July in the presence of Dr. Abercrombie, Professor Russell, Dr. Hunter etc.

The patient being seated in an ordinary chair, which posture, though inconvenient to myself, I preferred as most conducive to the prevention of suffocation from haemorrhage during the operation, I made an oblique incision by running a sharp pointed knife through the lip, from the right angle of the mouth to the base of the jaw, where I proposed to divide it, viz: at the 2nd bicuspid tooth, which had been removed the evening before. Having exposed the external surface of the bone at this point, I divided it partially with the saw, and easily completed what remained by means of the cutting pliers. The inferior coronary artery, which Dr. Ballingal had prevented from bleeding by compressing it in the lip, was then tied.

I next made a long semi-circular incision from the left angle of the mouth, in the direction of the base and ramus of the jaw and terminating over the condyle. Having secured the facial artery, and 2 transverse branches of the temporal artery, I dissected down the large flap thus formed quite to the neck, so as to let Dr. Ballingal feel the carotid lying in the muscular interspace and ready to be compressed if there should be occasion. I then made another curved incision in a similar direction, commencing from the mouth, at such distance above the former as to include a portion of the cheek, which was firmly adherent to the tumour; and having dissected up this flap, divided the masseter muscle, so as to expose the whole external surface of the tumour.

The next step was to divide the mucous membrane of the mouth. This rendered the tumour much more moveable, and enabled me to expose the coronoid process, divide the temporal muscle, and open the articulation at its fore part. I had then merely to cut closely round the condyle and detatch the pterygoid, mylohyoid, and other muscular connections.

The operation occupied twenty-four minutes, but all this time was not employed in cutting, as I frequently allowed a little respite, to prevent exhaustion from continued suffering. The patient bore it well, and did not lose more than 7 or 8 ounces of blood. His breathing was never in the slightest degree affected.

After placing a few folds of caddis in the great cavity left by the tumour, which weighed 4½ lbs, I brought the integuments together on the left side of the face, in a triangular form, and retained the edge in contact with the twisted suture. The incision on the right side was dressed in the same way. Two or three turns of a roller were then put round the chin and head so as to support the relaxed integuments.

The patient made no complaint of any sort after the operation. His pulse for the first two days was about 100, but soft, and gradually subsided to the natural standard. He slept well; had an appetite for his food viz: beef tea and whey, which were introduced into the pharynx through a funnel with curved tube and performed his excretions regularly. The whole of the caddis was removed by the third day, when the patient sat up and declared that he felt better than he did previous to the operation.

In concluding this case, I take the liberty of making a few general remarks on the mode of operating.

The patient ought certainly to be seated, since the blood will thus be prevented from running into his throat so as to delay the operation or even render tracheotomy necessary to prevent suffocation.

There is no advantage of tying the carotid artery previous to the extirpation. I was advised to do so, in the case above related, but declined on the following grounds:—

1. It is unnecessary, since the only arteries which must and ought to be cut are the facial, some of its branches, and some branches of the temporal.

2. It must exhaust the patient, especially when the tumour throws an obstacle in the way, as in Penman's case, where there was hardly any space left for applying a ligature. Thus in one of Dr. Mott's cases, the patient was so fatigued, as to require the delay of a day after the artery was tied.

3. It increases the danger, since it cannot be denied that there is always more or less risk of haemorrhage in the separation of a ligature from so large a vessel as the carotid.

4. It is of no use, since the anastomotic communications are so free that a ligature of the trunk is not sufficient to arrest the flow of blood from its branches. Thus in Dr. Mott's case abovementioned, the arteries which were cut during the operation required to be tied, and I have heard of a case, where the operator attempting to remove a tumour of the upper jaw, tied both carotids, and was still obliged to desist by the bleeding.

5. Any good effect that can be expected from the tying of the trunk may be obtained by compressing it after the integuments lying over it have been dissected off or divided.

For sawing through the lower jaw, I am quite sure that the chain saw, though recommended by a surgeon so experienced and judicious as my friend Dr. Cusack, is not the best instrument. The one I used has a straight blade 6½″ long and ½″ broad, with a straight handle. It will be found very useful in many different operations on the bones. It is not necessary to saw through the whole thickness of the bone. A pretty deep groove being made, the cutting pliers introduced into use with so much advantage to operative surgery by Mr. Liston, easily complete what remains. In this way I divided the jaw in less time than would have been required for passing the chain saw round it.

The external surface of the tumour should be completely exposed before proceeding further, since all the vessels which ought to be tied may then be tied in the first instance, and a free drain is afforded to the blood which oozes from the small branches.

The mucus membrane of the mouth being next cut by scalpel carried from the tonsil outwards, the tumour is rendered much more moveable and the surgeon will generally be able to free the coronoid process from its muscular connections. Should he fail in so doing, he ought to cut it across with the saw or pliers, and then depressing the tumour as far as possible, open the articulation in its fore part; after which he has merely to carry his knife close to the tumour and divide the remaining attachments.

I think Dr. Cusack is entitled to much praise for insisting in the propriety of opening the articulation from before, since a wound of the internal maxillary, or even the temporal is almost inevitable. Thus Mr. Liston in the case detailed in the last number of this journal, opened the joint from behind, and found it necessary to tie the common trunk of the temporal and internal maxillary—in short the external carotid. I do not mean to say that this proceeding was very dangerous to the patient or very difficult to so expert an operator as Mr. Liston, but I think that the great object of a surgeon should be to avoid cutting anything which it is not necessary to cut. And I think that the patient in this case would hardly have suffered the severe secondary haemorrhage which is mentioned in the relation referred to, if the superficial vessels merely had been divided.

It appears also that in Mr. Liston's case the ascending branches of the portio dura were cut, since the patient's eyelids were paralysed. Now this in all probability would not have happened if the articulation had been opened from before.

P.S. Penman is now quite well. His mouth is contracted to nearly natural size, and his appearance is not disagreeable. He is daily improving in articulation and can already express his wants pretty intelligibly. He has become much stronger, and is thinking of resuming his occupation.

75 George Street
Edinburgh
15th August 1828.

(Case of Osteo-sarcoma of the Lower Jaw removed by James Syme, F.R.C. Surgeons, Lecturer in Anatomy and Surgery etc.).

LORD LISTER'S LETTER

In 'Joseph, Baron Lister, Centenary Volume 1827-1927' Edited for the Lister Centenary Committee of the British Medical Association by A. Logan Turner in 1927, there is a chapter of 'Letters' and i.a. there is one written by Lord Lister to Principal Sir William Turner, describing various gifts presented to the University of Edinburgh for preservation:

'12 Park Crescent
Portland Place
1st February 1905.
'My dear Turner,
.... speaking of Mr. Syme, I possess some striking illustrations of his surgical character, which I should like to transfer to the

Museum of the University of Edinburgh. They refer to the famous case of huge fibro-cartilaginous tumour of the lower jaw, described by Mr. Syme in the *Edinburgh Medical and Surgical Journal* for 1828, and reproduced in his '*Contributions to the Pathology and Practice of Surgery*'. They are:

1. A beautifully prepared and mounted skeleton of the tumour. I am sorry to see, on looking at it today for the first time for many years, that the fine black dust of London has got in during its 27 years stay here, in spite of a well fitting glass case, and has much darkened the once beautiful whiteness of the preparation. Still, it is worth having in the Museum.

2. A coloured plaster cast of the head of the patient before the operation.

3. A portrait in oils of the patient also before the operation. I did not know of the existence of this till after Mr. Syme's death, when I found it in a cupboard in his consulting room. The fact that he had this portrait taken as well as the cast, shows the great importance he attached to the case, and also the confidence with which his sound pathological knowledge enabled him to look forward to success. This is all the more remarkable considering that Liston had refused to touch the case 3½ years before, and also that Mr. Syme, whose years went with the century, was a very young man. I have always understood that he was 27 years old at the time of the operation. The reference to the *Medical and Surgical Journal* in the "*Contributions*" does not mention the date of publication further than the year (1828). This could no doubt be cleared up by looking at the journal in the University Library. But whether he was 27 or 28 years old, he was very young. His skill and judgment as an operator are also well shown by this case, particularly when his account of it is read.

The patient, Robert Penman, afterwards went to America, and came over on a visit to Scotland during the early time of my first stay in Edinburgh, about 1855 or nearly 30 years after the operation, in perfect health and with the deformity wonderfully masked by a bushy beard. I have a photograph of him taken at the time and I should like it to go with the other things .... I have given directions to my executors that these things should be sent there on my decease. But I feel that there would be a very great risk of the tumour being spoiled before they arrive at their destination. It has occurred to me that perhaps your son here would take charge of them in one of his visits to you....

Very truly yours,
Lister.'

Unfortunately, I did not come across the coloured plaster cast of Penman's head mentioned in Lord Lister's letter, otherwise I would have photographed it also.

In the light of all the advances made in anaesthesia, surgery and treatment of wounds and, more recently, the antibiotics, in the past 130 years, and as this case described by Syme was also in the pre-chloroform and pre-Listerian eras, this record of an operation done 8 years before the Great Trek in Southern Africa is indeed one of great interest. The publication of Mr. Schrire's case stimulated me to search through my collection of Edinburgh records for these items associated with the Penman case of Mr. Syme.

They are here submitted as gems of great historic and clinical interest.

ABSTRACT : UITTREKSEL

FAR EAST INFLUENZA

Smith, C. E. G., Turner, L. H. and Helliwell, C. J. V. 1957.

Far East Influenza. British Medical Journal—**1**, 1412.

This is the first clinical report of Asiatic or Asian 'flu and comes from Kuala Lumpur.

'The disease was made a notifiable one in the Malayan Federation on May 4. By May 10 notifications were being received from most of the large towns; but the rural areas were not widely affected until about two weeks later and in many the peak is only now being reached. In each town the incidence has risen sharply during the first four or five days and has then been maintained for about three weeks.'

The majority of patients early in the epidemic were poorer people living in the most crowded and least healthy environments. Since then the disease has progressively affected those living in better circumstances, so that in the fourth and fifth weeks of the epidemic more and more patients from the upper class of Asians and among the Europeans have been seen.

Clinical Features

The clinical severity of the disease has varied widely, but a typical attack has the following course. Especially in children, the first complaint is usually of thirst followed in 6-12 hours by a very sore throat. On examination, a bright red velvety imflammation is characteristically confined to the posterior pharyngeal wall. About this time the temperature is around 102°F (38·9°C) and the pulse about 120 per minute. A generalized headache develops 3-6 hours later and in adults and adolescents is often accompanied by aching, particularly in the lower chest and lower back. Aches are uncommon in children, whose main discomforts are the sore throat and a 'floating', 'bloated' headache. Tonsillar enlargement without suppuration may occur during the next 24 hours, usually in patients with chronic tonsillitis. Dry cough is common at this stage, but no crepitations have been detected in the lungs of uncomplicated cases. By the third day the cough is brassy and associated with tracheitis. During the second 24 hours the fever is maintained, but the sore throat disappears and the headache and muscular aches diminish. Recovery is usual by the fourth day, and most patients return to work after about 5 days' absence. Vomiting has not been marked except in those intolerant of salicylates or given solid food during the first 24 hours.

About 10% of patients return after the third or fourth day with secondary bronchitis, tonsillitis, etc. A few patients have had a short recurrence of fever about the seventh or eighth day.

Treatment

Symptomatic treatment with salicylates has been very effective when combined with strict bed rest for 2-3 days, a bland diet, and copious fluids. Intramuscular chloramphenicol has been given to a number of severe cases with apparent benefit, but controlled evaluation of this observation has not been possible.

THE D. P. MARAIS SANTA CENTRE AT WESTLAKE

On 4 July 1957 the first patients were admitted to the D. P. Marais Tuberculosis Centre at Westlake, Cape, which has been established by the Cape Tuberculosis Council acting on behalf of the South African National Tuberculosis Association.

The new Centre consists of 32 existing blocks, part of the extensive encampment at Westlake originally built by the British Government during World War II and ceded to the Union Government after the war. Conveniently sited as to water, power and communications, these buildings now include the Westlake Chest Hospital (for Europeans) of the Union Government, the Dr. Stals Memorial Sanatorium (for Coloured females) of the Cape Divisional Council and the new D. P. Marais SANTA Centre (for Coloured males), besides blocks occupied by the Union Government for various purposes.

Taking its place as an integral part of the clinic-hospital set-up of the Cape Peninsula, its proper function will be to speed up the turn-over of beds in the chest hospitals. It will take over cases from the tuberculosis clinics immediately after diagnosis has

been established and will control and treat them until there is a hospital bed vacant, or until they are discharged to the clinic for convalescent observation and control. It will make an immediate end of the waiting list for tuberculous Coloured males, a matter which has been a standing reproach for many years. This quick and effective handling of the case is the very basis of success in tuberculosis work—and is also the essence of the rationale of the Edinburgh Plan as conceived and elaborated by the late Sir Robert Philip, the centenary of whose birth is being celebrated this year.

After prolonged negotiations with Government departments, the buildings have been made available to SANTA, who have repaired and equipped them. The local authorities concerned, viz. the Cape Town City Council (Dr. E. D. Cooper, MOH) and the Cape Divisional Council (Dr. J. P. de Villiers, MOH), are accepting responsibility for the cost of the first 130 patients and will recover 7/8ths of this expenditure from the Union Government.

Mr. C. E. J. van Vlaanderen, hitherto in charge of the FOSA Settlement (SANTA) at the Cape, has been appointed as the first Warden. His knowledge and experience have been of great value at the outset of this project. Dr. P. Scher, Medical Superintendent of the adjoining Westlake Chest Hospital, has kindly undertaken to provide the necessary medical advice.

While the occupation of only 100 beds is at present guaranteed, it will be possible, subject to the necessary financial provision, to fill the Centre up to 320 beds or more. To this end the committee of management, drawn from medical and business members of the Cape Province Tuberculosis Council, will bend all its energies as it calls on the contributing public, through SANTA, for fullest support in this significant effort.

By unanimous resolution approved by SANTA, the Executive of the Cape Tuberculosis Council decided to name this project the D. P. Marais SANTA Centre in recognition of the long and close association of Dr. D. P. Marais with the tuberculosis campaign in South Africa. The first anti-tuberculosis movement in South Africa was founded in 1904 as the Association for the Prevention of Consumption, of which Dr. D. P. Marais was hon. secretary under the late Dr. A. Jasper Anderson (MOH of Cape Town) and later chairman. About 1925 the Association was reconstituted as the Cape Province Tuberculosis Council, which became one of the foundation pillars of SANTA. Dr. Marais' public service in the anti-tuberculosis field has covered a period of 50 years and dates from a public lecture which he gave in 1907 in the old Town House of Cape Town (now Michaelis Gallery) under the chairmanship of the late Dr. H. A. Moffat.

It is to commemorate this long and faithful devotion to a cause that the Council have named the new Centre after him.

PASSING EVENTS : IN DIE VERBYGAAN

Income Tax. An Article *Income Tax as it effects the Medical Practitioner*, will appear in next week's issue of the *Journal* (27 July 1957).

* * *

Mr. C. C. Wiggishoff, M.B., B.Ch. (Oxon.), F.R.C.S. (Eng.), F.R.C.S. (Edin.), of Bhekulwandhle, Gillits, Natal, lately first senior registrar at St. Peters Hospital for Stone, London, has been appointed Senior Resident, Department of Urology, University of Illinois, Chicago.

* * *

Association of Surgeons in South Africa. The annual general meeting of the Association of Surgeons of South Africa will be held on Wednesday 18 September 1957 at 2.15 p.m. at the South African Medical Congress, Durban. The agenda includes the following items: Minutes and matters arising; Reports of the hon. secretary and treasurer; Election of office bearers for the executive committee; Proposed fund for visiting surgeons; and general. Notices of motion must be received by the honorary secretary (Dr. K. Colsen, Medical House, 5, Esselen Street, Hospital Hill, Johannesburg) not later than 3 weeks before the annual general meeting.

* * *

Journal Supplement. Members of the Medical Association of South Africa are reminded that if they have not already done so they will receive (without charge) a copy of the supplement to the *South African Medical Journal* known as 'Medicine in South Africa—Medisyne in Suid-Afrika (1957)' on application to the Secretary of the Association, 35 Wale Street (P.O. Box 643), Cape Town. The supplement comprises the English version of a series of 14 articles by South African authors which have been published in the Portuguese Medical Journal *O Medico* under the auspices of the South African Council for the Exchange of Medical Sciences, together with messages from His Excellency the Portuguese Ambassador (General A. Pinto) and the Hon. J. H. Viljoen (Minister of Arts, Sciences and Education and Minister of Health). This supplement, which consists of 157 pages, has been sponsored and produced by the South African Council for the Exchange of Medical Sciences.

* * *

Dr. Emilia Krause. As a member of the Council of the International Society for the Welfare of Cripples, Dr. Emilia Krause, of Bloemfontein, is attending the 7th World Congress of this Society in London in July; where she will contribute a paper on *Education in Cripple Care; the medical aspect.* Dr. Krause has also been attending the 4th International Poliomyelitis Conference which was held this month in Geneva.

* * *

Dr. Louis Meyerson, M.B., Ch.B. (Rand), D.O. R.C.P. and S. (Eng.), Ophthalmic Surgeon, has changed his address from 606-608 Clinical Centre, Wanderers St., Johannesburg, to 139 Lister Building, Jeppe St., Johannesburg. The telephones remain unchanged, viz. rooms 23-7785, residence 42-1049.

* * *

Unie van Suid-Afrika. Departement van Gesondheid. Aangifte van ernstige epidemiese siektes en poliomiëlitis in die Unie gedurende die tydperk 28 Junie—4 Julie 1957.

	Poliomiëlitis				
	Bl.	*Nat.*	*Kl.*	*As.*	*Totaal*
Transvaal	—	1	—	—	1
Kaapprovinsie ..	4	1	4	—	9
Oranje-Vrystaat ..	—	1	—	—	1
Natal	—	—	—	—	—
	—	—	—	—	—
Totaal	4	3	4	—	11

Pes, Pokkies, Tifuskoors. Geen.

REVIEWS OF BOOKS : BOEKRESENSIES

PULMONARY EMPHYSEMA

Pulmonary Emphysema. Edited by Alvan L. Barach, M.D. and Hylan A. Bickerman, M.D. Pp. x + 545. 185 Illustrations. 80s. net. Baltimore: Williams & Wilkins Company. London: Baillière, Tindall and Cox, Ltd. 1956.

Contents: 1. Pathogenetic and Allied Influences in Chronic Pulmonary Emphysema. Alvan L. Barach. 2. The Application of Respiratory Physiology to Therapeutic Procedure in Pulmonary Emphysema. Alvan L. Barach. 3. Restoration of Diaphragmatic Function and Breathing Exercises. Alvan L. Barach. 4. Senile Emphysema. Hylan A. Bickerman. 5. Corticotropin and the Adrenocorticosteroids in the Treatment of Pulmonary Emphysema. Hylan A. Bickerman. 6. Pharmacologic Therapy in the Management of Pulmonary Emphysema. Hylan A. Bickerman. 7. Methods of Aiding Bronchial Drainage in Pulmonary Emphysema. Gustav J. Beck. 8. Aerosol Therapy in the Management of Bronchopulmonary Infection, Including Use of Exsufflation. Edwin R. Levine. 9. The Mechanics of Breathing. Howard G. Dayman. 10. Administration of Bronchodilator Aerosols and the Use of Intermittent Positive Pressure Breathing (IPPB). H. Drew Miller, Ward S. Fowler and Frederic Helmholz, Jr. 11. Physiologic

Considerations in Management Relative to the Development of Acidosis and to the Work of Breathing. James K. Alexander. 12. The Role of Infection in Chronic Hypertrophic Pulmonary Emphysema. Vernon Knight and Arthur C. White. 13. The Diffusing Capacity of the Lungs in Patients with Pulmonary Emphysema. Richard L. Riley. 14. Respiratory Acidosis. Reuben M. Cherniack. 15. Cor Pulmonale in Chronic Pulmonary Emphysema. Dickinson W. Richards, Jr., and Alfred Fishman. 16. Surgical Procedures in Pulmonary Emphysema. Ralph A. Deterling. 17. Respiratory Function Tests. George R. Meneely and James K. Callaway. 18. Comments on Preceding Chapters. Alvan L. Barach. Index.

This is an authoritative monograph contributed by 18 writers. Its scope reaches far beyond the mere title of Pulmonary Emphysema, and covers adequately every phase of the physiology, the dynamics, and the effects of pathology on the respiratory processes. It makes a strong appeal for the establishment of a 'lung station', i.e. a place for the complete assessment of lung function as affected in health and disease, in every big hospital, analogous to the 'heart station'.

The development of this work in the last decade has been remarkable. Out of the pure scientific research of the physiological laboratory have developed practical and clinical methods which are of immense importance in understanding the mechanisms involved in health as well as in disease of the respiratory system. In a manner very similar to the evolution of basal metabolism from a matter of largely scientific laboratory interest to a thoroughly practical application with portable apparatus at the bedside, this new work has developed to take its place in practical clinical equipment. But so specialized is this new work that its appreciation almost demands a dictionary of terms,—a new language, such as one encounters in the literature of psychiatry.

The chapters on pulmonary physiology, chemistry, and dynamics, require careful perusal, but those on the practical and clinical application are helpfully clear. Pulmonary emphysema, once the despair of the physician, is now more clearly understood and can be controlled with more certainty than previously. The medical management as described is that carried out at the special clinic in the Presbyterian Hospital (New York) by Barach, Bickerman and Beck. Apart from the highly technical chapters on pulmonary function and its assessment, there is much of practical and therapeutic value in the chapters on treatment.

In keeping with the high scientific value of this work, each chapter or series is followed by a selective bibliography. Selection has been necessary since, in the last two decades, 'over 700 authors have published articles which attracted at least enough attention to be quoted one or more times in other papers, and the leading articles were disseminated among 43 different medical journals'.

This then is a really worth-while work, an eminently well-rounded treatise which every chest specialist should possess. Its format and printing leave nothing to be desired, and reflect the usual high quality one has come to expect from the firm of Ballière, Tindall and Cox.

D.P.M.

TOPECTOMY

Studies in Topectomy. Edited by Nolan D. C. Lewis, M.D., Carney Landis, Ph.D., D.Sc. and H. E. King, Ph.D. Pp. viii + 248. $6.75. New York and London: Grune & Stratton, Inc. 1956.

Contents: Contributors. 1. Editorial Introduction. 2. Surgical Procedure. 3. Physiological Effects. 4. Vestibular Function. 5. Autokinesis. 6. Psychometric Studies. 7. Complex Mental Functions. 8. Activity: A Time-sampling Study. 9. Psychophysiology. 10. Psychosurgery and Sexual Behavior. 11. Psychiatric Effects. 12. Independent Psychiatric Evaluation. 13. Social Service.

This monograph is a further attempt to clarify the functions of the frontal lobe in man, and the effects of psycho-surgery of a special type on chronic psychotic patients.

From the surgical side two kinds of surgical ablations were carried out. In approximately one-half a block of cortex was removed bilaterally from the rostro-medial aspect of the superior portion of each frontal lobe. This is designated as 'superior' topectomy. In the other half an equal weight of cortex was removed bilaterally from the orbital (inferior) aspect of the frontal lobes, a procedure designated as 'orbital' topectomy.

These patients were studied before and after psycho-surgery by different teams of researchers in the fields of psychiatry, physiology and psychology, and the findings are reported in the subsequent chapters.

After reading these various reports one is again struck by the difficulty in assessing the results of any form of psycho-surgery.

One fact however does come out clearly and that is that psycho-surgery, in this instance topectomy, has a place in the treatment of psychiatric patients, provided that they are carefully selected.

The book should prove of interest and benefit to psychiatrists and to all other members of the medical profession who are interested in psycho-surgery.

H.L.deV.H.

PHARMACY LAW

A Manual of Pharmacy Law. By T. W. Price, Ph.D., M.A. (Cantab.), B.A., LL.B. (South Africa), and R. Pannall Dip. Pharm. (S.A.); M.P.S. Pp. xxiii + 232. 45s. (Delivery charge extra). London: Butterworth & Co. (Publishers) Ltd. South African Office: Butterworth & Co. (Africa) Ltd., P.O. Box 792, Durban. 1956.

Contents: Foreword. Preface. Table of Contents. List of Abbreviations. Table of Statutes. Table of Cases. I. The Registration and Professional Discipline of Pharmacists. II. Unprofessional Conduct. III. The Pharmacist's Contracts. IV. Delictual Liability of the Pharmacist. V. Criminal Liability of the Pharmacist. VI. Pharmaceutical Standards. VII. Poisons and Dangerous Drugs. VIII. Alcoholic Liquors and the Pharmacist. IX. The Pharmacist's Weights and Measures. X. The Pharmacist's Licences and Shop Hours. XI. The Pharmacist as an Expert Witness. Appendix—Notes for Students. Index.

This is a useful book in so far as it collects material from many sources into a handy manual. It does not purport to cover original ground. Nevertheless a book on the law relating to the pharmacy profession is welcome. In this regard the authors have been faced with a difficult task. In present-day practice pharmacists outside hospitals and research laboratories have become retail traders in ethicals, who also compound an occasional script. That no doubt is the reason for the inclusion of certain aspects of the law of contract which would otherwise be out of place in such a book. In this regard it is well for the pharmacist to remember that his contract of sale differs little from that of the greengrocer or anyone else. He would be unwise to rely on the inevitably limited treatment in this manual were he to be involved in a legal difficulty. The danger of a book such as this is that it tends to make sea-lawyers of the lay public.

On the other hand pharmacists always have before them the fear of a claim for damages as a result of negligence. This aspect is properly dealt with, including sound advice about the necessary cover by insurance. The section on defamation seems unnecessary; by and large today this is a delict involving politicians and newspapers. The section on vicarious responsibility is inadequate. All commercial pharmacists employ assistants, qualified and unqualified. The responsibility of the pharmacist for actions of his employees is of daily worry to him. This aspect is hardly considered. The section deals with the vicarious responsibility of hospitals for pharmacists on the staff, but not with the far more frequent situation of the pharmacist who owns his own business and may be held liable for the negligence of his assistants.

In the section dealing with the criminal liability of the pharmacist there is surprisingly no reference made to section 87 of the Medical, Dental and Pharmacy Act, 1928. This important section makes the pharmacist liable for acts of his employee, in the sale of certain poisons and habit-forming drugs. Pharmacists will remember a case in Natal—R. v Rubin 1949 (1) P.H.H. 101—which considered the liability of a pharmacist for an act of his employee.

The case law covered in this book is wide. There seems little point however in referring to American cases, when such reports are not available in South Africa. The book refers to all legislation affecting the pharmacy profession in South Africa.

The literature devoted to pharmacy is limited, and this book certainly widens the field. It is handy in size and neatly produced. Pharmacists will find it useful in checking up a point of law quickly without extensive research. Legislation affecting pharmacists has until now been scattered, and has been inaccessible to all but the lawyer. This book collects the various sources.

A.P.

PERIPHERAL VASCULAR DISORDERS

Diagnosis and Treatment of Peripheral Vascular Disorders. The clinician's guide to disorders of the arterial, venous and lymphatic systems. By David I. Abramson, M.D., F.A.C.P. Pp. xv + 537. 82 Figures. $13.50. New York: Paul B. Hoeber, Inc. 1956.

Contents: List of Tables. Preface. Acknowledgements. *Part One: Differential Diagnosis of Symptoms and Signs.* I. Differential Diagnosis of Pain in the Extremities. II. Procedures for Study of Arterial Circulation in the Extremities: 1. Tests

Reflecting State of Cutaneous Arterial Circulation. III. Procedures for Study of Arterial Circulation in the Extremities: 2. Procedures for Determining State of Main Arteries. IV. Procedures for Study of Arterial Circulation in the Extremities: 3. Tests for Removal of Vasomotor Tonus and for Determination of State of Muscle Circulation. V. Procedures for Study of Venous Circulation in the Extremities. VI. Differential Diagnosis of Physical Findings: 1. Excessive Sympathetic Tonus; Abnormal Neurologic Signs; Entities Associated with Petechiae and Ecchymosis; Cutaneous and Subcutaneous Masses; Swelling. VII. Differential Diagnosis of Physical Findings: 2. Ulceration; Gangrene. *Part Two: Peripheral Vascular Diseases.* VIII. Vascular Entities Primarily Affecting the Arterial Tree: 1. Classification; Raynaud's Disease. IX. Vascular Entities Primarily Affecting the Arterial Tree: 2. Chronic Occlusive Arterial Vascular Disorders. X. Vascular Entities Primarily Affecting the Arterial Tree: 3. Complete Occlusion of Arteries. XI. Vascular Entities Primarily Affecting the Arterial Tree: 4. 'Collagen Vascular Disorders'. XII. Vascular Entities Primarily Affecting the Arterial Tree: 5. Therapeutic Procedures in Conditions with Permanent Arterial Impairment. XIII. Vascular Disorders Affecting the Venous System: 1. Diseases of the Superficial Veins. XIV. Vascular Disorders Affecting the Venous System: 2. Thrombosis of Deep Venous System. XV. Vascular Disorders Affecting the Venous System: 3. Pulmonary Embolism. XVI. Vascular Disorders Affecting the Venous System: 4. Clinical Manifestations of Venous Stasis and Their Treatment. XVII. Vascular Entities Produced by Trauma or Noxious Agents: 1. Conditions Resulting from Injury to Main Vessels. XVIII. Vascular Entities Produced by Trauma or Noxious Agents: 2. Posttraumatic Painful Lesions. XIX. Vascular Entities Produced by Trauma or Noxious Agents: 3. Conditions Arising from Cold Injury. XX. Vascular Entities Produced by Trauma or Noxious Agents: 4. Syndromes Resulting from Compression of Subclavian Vessels and Brachial Plexus. XXI. Rare Vascular Disorders Affecting the Extremities. XXII. Disorders of the Lymphatic System. XXIII. Congenital Anomalies. XXIV. Peripheral Vascular Entities not Affecting the Extremities. XXV. Technics of Therapeutic Measures Requiring Special Equipment or Skill. *Part Three: Anatomic, Physiologic, Pharmacologic, and Pathologic Considerations of the Peripheral Circulation.* XXVI. Anatomy and Physiology of Blood Vessels in the Extremities. XXVII. Sympathetic Nervous System. XXVIII. Variations in Circulation in the Extremities under Different Physiologic and Pathologic States. XXIX. Intravascular Blood Clotting and its Prevention. XXX. Pharmacologic Action of Agents that Play a Role in Peripheral Vascular Disorders. Appendix: Sources of Proprietary Drugs, Instruments, and Surgical or Laboratory Supplies. Index.

The author emphasizes that his book is not intended for the specialist, but for the busy family physician. We agree that on the whole he has succeeded in this intention, yet his book still runs into 500 pages. The time seems ripe for someone to give us a small 'handbook' on peripheral vascular diseases. However, the style of this book is eminently readable and the subject matter made understandable by the use of numerous charts and tables.

The author has avoided theory and academic discussion in order to provide a practical guide to the management and treatment of vascular disorders. Unfortunately, the information is often phrased in vague terms, such as, the life expectancy in abdominal aneurysms is 'much lower' than in the normal population, or 'the sympathetic nerves appear to have a tendency to regeneration'.

Seeing that the book is intended for general practitioners one would have liked a more detailed discussion of the indications and complications of the simpler surgical manoeuvres, for example stellate blocks and similar procedures.

The reviewer feels that the value of treating varicose veins by stripping is not given sufficient prominence in the discussion on injection therapy. Similarly the technical details concerning arteriography are not sufficiently concise. Few will agree to the use of 30 c.c. of '35% *or* 70% contrast medium for the brachial and 50 c.c. of 70% for femoral arteriography'. To use a 70% solution for venography is asking for trouble.

The subject matter is divided into 3 parts, of which the first deals with the differential diagnosis of symptoms and signs, and the second presents the clinical disorders arranged according to a convenient classification, with details of treatment for each condition. The emphasis is on simple effective measures which the author has found useful in his personal experience. The final section of the book summarizes the clinical anatomy and physiology of the peripheral circulation.

The book is beautifully produced and well illustrated, and a limited bibliography is appended to each chapter.

Keeping the limitations mentioned above in mind, the book can be recommended to the practising physician.

R.H.G.

SCIENTIFIC INVESTIGATION OF CRIME

The Scientific Investigation of Crime. By L. C. Nickolls, M.Sc., A.R.C.S., D.I.C., F.R.I.C. Pp. xiii + 398. 225 Figures. 57s. 6d. + 1s. 6d. delivery charge. London: Butterworth & Co. (Publishers) Ltd. South African Office: Butterworth & Co. (Africa) Ltd., P.O. Box 792, Durban. 1956.

Contents: Foreword by Sir John Nott-Bower, K.C.V.O. Introduction. 1. The Laboratory. 2. Scenes of Crime. 3. Dirt, Dust and Debris. 4. Identification of Traces of Inorganic Material. 5. Identification of Traces of Biological Material. 6. Instrument Marks. 7. Footprints and Tyre Impressions. 8. Erased Identification Marks. 9. Bloodstains. 10. Seminal Stains and Stains of other Body Fluids. 11. Abortion. 12. Arson and Spontaneous Combustion. 13. Firearms and Cartridges. 14. The Examination of Documents. 15. Blood and Urine Alcohol Determination. 16. Toxicology. Index.

This book details the scientific investigations associated with criminal offences. The role of the laboratory in elucidating evidence is well described. The author is a highly qualified scientist, skilled in the techniques used in the laboratory. The equipment of a modern forensic laboratory is varied and complex, including such apparatus as cameras, microscopes, biochemical reagents, X-ray machines and others. The author describes all the equipment used in a forensic laboratory and then proceeds to deal with the investigations necessary to prove any exhibit in specimen, suspected of being linked with the offence, as being in fact associated with the crime itself.

The methods used to identify organic material, instruments, stains, firearms, documents and other specimens, are described very clearly. There is also a chapter on toxicology. Very useful chapters are those on the examination of documents, and on firearms and cartridges.

The author very wisely does not deal with pathological investigations, except the identification of blood and its derivatives, and of semen. He has also avoided the snare of interpreting the law. This is difficult enough for lawyers, but such difficulties sometimes fail to deter others.

The author writes with a background of very wide personal experience, which is evident throughout the book, and this gives it its main value. He has had a lifetime of experience working in forensic laboratories in England and for the last 6 years has been Director of the Metropolitan Police Laboratory at New Scotland Yard.

This book is thoroughly recommended to every forensic laboratory worker. To the layman interested in the detection of crime it will also make interesting reading. The author has a knack of presenting very technical matters in an interesting easy style. Forensic scientists will find the book useful. Lawyers will find in it a vast store of helpful material for the conduct of their criminal trial work. All in all a good book well written and well produced, with numerous clear and explicit illustrations. A.P.

CORRESPONDENCE : BRIEWERUBRIEK

PHARMACEUTICAL ADVERTISING

To the Editor: In the fourth paragraph of your editorial[1] under this title in the issue of the *Journal* dated 29 June 1957 you refer quite rightly to the great service rendered by the pharmaceutical houses of the United States of America to research and therapeutics. The paragraph however is inadvertently slightly misleading as similar support is being made on no mean scale by the great pharmaceutical houses elsewhere.

In my own department, for example, one of the Swiss pharmaceutical firms has very generously supported basic researches which are in no way related to its medicinal products. Likewise one of the British houses has made a donation of valuable equipment without any obligation or conditions. The department has, of course, also received valuable assistance from American houses.

J. M. Watt

Department of Pharmacology and Therapeutics
University of the Witwatersrand
Johannesburg

5 July 1957

LARGE FUNDS DEVOTED TO RESEARCH

To the Editor. Congratulations on your editorial[1] of 29 June, because it dealt bravely with a controversial subject. I was, however, surprised to read that 'especially in the

United States' some of the great pharmaceutical houses devote large funds to research.

I do not know whether, when making such a statement, you had at your disposal figures from the States, Great Britain and Switzerland on which to base your contention. Certainly, if you singled out one country as being specially generous in aiding medical research, you must have had your reason but I am certain you will receive quite a number of letters from individual firms challenging your statement.

I do so now on behalf of my parent company domiciled in a small European country which is not in the propagandistic limelight of world events.

G. Reuss, Ph.D.
Director.

Roche Products (Pty) Ltd.
P.O. Box 6158
Johannesburg
5 July 1957.

A PAT ON THE BACK

To the Editor. We would like to forward our congratulations on your editorial,[1] which appears in the current issue of your *Journal*. After receiving many hard knocks from the profession itself, it is a pleasant change to receive a pat on the back from a leading medical journal.

J. R. Oversby
South African Manager.

The Crookes Laboratories
P.O. Box 1573
Johannesburg
3 July 1957.

1. Editorial (1957) S. Afr. Med. J., **31**, 635.

CONTINENTAL FIRMS' SUPPORT

To the Editor. Although we very much appreciate what you had to say in your editorial of the *Journal* of 29 June, we cannot but take exception to the following part of the first sentence in the fourth paragraph: 'especially in the United States'. It is quite probable that owing to the fact that continental pharmaceutical houses like Sandoz Limited in Basle do support in the first instance research workers, medical schools and universities in their own countries and on the continent generally speaking, and that therefore much of the work is not published in English, their contribution to independant scientific research has not come to your notice as much as work supported by firms in English-speaking countries.

Nevertheless it is a fact that the continental firms are contributing to a very high extent to the cost of maintaining research institutions in their own countries and abroad, and every reader who is acquainted with American literature will also find that those continental firms are often quoted as having supported research work carried out in the United States. We would also like to mention that Sandoz for one have also been actively supporting and are still supporting research work in this country.

Paul G. Stein
Alex. Lipworth Limited
Sandoz Pharmaceutical Department

P.O. Box 4461
Johannesburg
4 July 1957

A DISCLAIMER

To the Editor: In the *Journal* of 23 March 1957 you published a letter by J. H. van Eck Kirsten. This letter evoked a few replies—a fairly moderate one by Dr. W. Steenkamp[2] who conveniently prefixed the title of 'Professor' to the name of the author, and a rather acid reply by Dr. Ronald Singer.[3]

This correspondence was brought to my notice after my return to South Africa, and I wish to state emphatically that I am not responsible for the letter written by J. H. van Eck Kirsten. As you know, I paid a visit to your office on 28 June 1957 when I asked to see the original letter. This unfortunately could not be produced by your staff and was stated to have been destroyed. A check in the Medical Register revealed that there is no such name registered, but my name bears the closest resemblance to that of the author. Please note the initials and spelling of my name below.

The reason for writing this disclaimer is that anybody at the Royal College of Surgeons who reads Dr. Singer's letter without being able to understand the letter by J. H. van Eck Kirsten must of necessity conclude that derogatory things were said although I frankly cannot find any such implication in it. Furthermore, everybody who spoke to me about this matter was under the impression that I am the author of the letter. I do not see why I should stand up to a barrage that should have been directed on to a different target.

I sincerely hope that the author will come forward to clear up this case of mistaken identity.

J. F. van Eyk Kirsten

Department of Anatomy
University of Stellenbosch
9 July 1957

1. Kirsten, J. H. van Eck (1957): S. Afr. Med. J., **31**, 296.
2. Steenkamp, W. (1957): *Ibid.*, **31**, 376.
3. Singer, R. (1957): *Ibid.*, **31**, 348.

NURSING ACT 1957

To the Editor: Mrs. Ramusi's trenchant letter of 4 May[1] appears to be the first intimation in a South African medical journal of the nature and importance of the Nursing Bill.* She draws attention to a series of intended discriminations against non-European nurses by the Bill, and to previous discriminations by the South African Nursing Council and the Nursing Association.

The standards of training and performance for nurses are, of course, of immediate concern to medical services and the medical profession. In addition there is an important clause in the Nursing Bill, not mentioned by Mrs. Ramusi, which affects the medical profession directly:

'49. Any person who causes or permits any white person who is registered or enrolled' (as a nurse under this Act) 'to be employed under the control or supervision of any person who is not a white person, in any hospital or similar institution or in any training school, shall be guilty of an offence and liable on conviction to a fine not exceeding two hundred pounds.*

This clause can only be interpreted as direct discrimination against non-European doctors.

It is surprising to us that, as far as we can discover, the medical profession, officially or otherwise, has published not a word on this matter. May we ask that sympathetic colleagues should lose no time in taking up an issue which is already desperate?

Zena Stein†
Mervyn Susser
Albert Kushlick
Sidney Leibowitz
J. G. Thuynsma
B. Abrams

London
England
2 June 1957

1. Ramusi, M. (1957): S. Afr. Med. J., **31**, 439.

* The Bill is now gazetted as the Nursing Act. Clause 49 of the Bill was amended and now reads in the Act as follows:
'49. Any person who, except in cases of emergency, causes or permits any white person who is registered or enrolled or who is registered under section 14 or enrolled under section 15, to be employed under the control or supervision of any registered or enrolled person who is not a white person, in any hospital or similar institution or in any training school, shall be guilty of an offence and liable on conviction to a fine not exceeding £200.'

The expression 'any registered or enrolled person' means any nurse or midwife or auxiliary nurse or midwife registered or enrolled under this Act (section 12). It does not refer to medical practitioners, who are not registered under this Act.—*Editor.*

† All these signatories hold the degrees of M.B., B.Ch. (Rand).